9/28/2004

ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:796898 CAPLUS
ENTRY DATE: Entered STN: 14 Nov 2000
TITLE: Photochemical and electrochemical control of recognition processes. Toward a three-pole molecular switch.
AUTHOR(S): Goodman, Allan J.; Rotello, Vincent
CORPORATE SOURCE: Department of Chemistry, University of Massachusetts, Amherst, MA, 01003, USA
SOURCE: Abstracts of Papers, 220th ACS National Meeting, Washington, DC, United States, August 20-24, 2000 (2000) ORGN-395
CODEN: 69FZC3
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
ABSTRACT:
Mol. devices are increasingly attractive for applications in information storage, mol. shuttles and switches. One key goal in the creation of devices is the incorporation of multiple inputs into the mol. system. To achieve this goal we have created a synthetic receptor 1 that utilizes orthogonal photochem. and electrochem. to control mol. recognition processes. In 1 a photoswitchable aromatic stacking unit is used as a photochem. input to modulate the binding of the **naphtalimide** guest 2. Redox modulated recognition then supplies the second, orthogonal, input. Synthesis and recognition studies of this prototypical device will be presented.

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1974:554514 CAPLUS
DOCUMENT NUMBER: 81:154514
ENTRY DATE: Entered STN: 12 May 1984
TITLE: New intermediates and dyes for synthetic polymer fibers. 4-(4-Methoxyanilino)-3-nitro-1, 8-**naphtalimides**
AUTHOR(S): Kadhim, Abla M.; Peters, Arnold T.
CORPORATE SOURCE: Sch. Colour Chem. Colour Technol., Univ. Bradford, Bradford, UK
SOURCE: Journal of the Society of Dyers and Colourists (1974), 90(5), 153-7
CODEN: JSDCAA; ISSN: 0037-9859
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 40-6 (Dyes, Fluorescent Whitening Agents, and Photosensitizers)
ABSTRACT:
Napthalimide dyes I (R = H, Bu, Bz, COSEt, CSNHPh, Me, Ac, CO2Et, CONHPh) and II (R1, R2 = H, Me, Bu) were prepared by various routes starting with 4-halonaphthalene-1,8-dicarboxylic anhydride and dyed acetate and polyester fibers fast orange and yellow shades resp. Thus, 4-chloronaphthalenedicarboxylic anhydride was nitrated to give 4-chloro-3-nitronaphthalene-1,8-dicarboxylic acid, which was refluxed with 4-MeOC6H4NH2 in EtOH for 2 hr, H2NCH2CH2CH2OH added to the cooled reaction mixture, and refluxed for 1.5 hr to give naphthalimide dyes I(R = H) [52821-25-7].

SUPPL. TERM: napthalimide disperse polyester dye; acetate fiber dye; methoxyanilinonitronapthalimide disperse dye
INDEX TERM: Dyes
((methoxyanilino)nitronaphthalimide derivs., acetate and polyester fibers)
INDEX TERM: Acetate fibers
Polyester fibers
ROLE: USES (Uses)

(dyes for, (methoxyanilino)nitronaphthalimide derivs. as)
INDEX TERM: 81-86-7 4053-08-1
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(nitration of)
INDEX TERM: 52821-19-9P 52821-20-2P 52821-21-3P 52821-22-4P
52821-23-5P 52821-24-6P 52821-26-8P 52821-27-9P
52821-28-0P 52871-22-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
INDEX TERM: 98-88-4 103-71-9 103-72-0 541-41-3 2941-64-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (hydroxypropyl)(methoxyanilino)nitrona
phthalenedicarboxylic anhydride)
INDEX TERM: 156-87-6 5332-73-0 16499-88-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (methoxyanilino)nitronaphthalenedicarb
oxylic anhydride)
INDEX TERM: 104-94-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromonitronaphthalenedicarboxylic
anhydride)
INDEX TERM: 52821-06-4 52821-07-5 52821-08-6 52821-09-7
52821-10-0 52821-11-1 52821-12-2 52821-13-3
52821-14-4 52821-15-5 52821-16-6 52821-17-7
52821-18-8 52821-25-7
ROLE: USES (Uses)
(spectra and fastness on polyester fibers of)

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=> d his

     (FILE 'HOME' ENTERED AT 16:36:25 ON 30 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 16:36:39 ON 30 SEP 2004
L1             STRUCTURE UPLOADED
L2           235 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 16:37:18 ON 30 SEP 2004
L3           177 S L2
L4             1 S L3 AND AMMONIUM
L5             0 S L3 AND NAPHTALIMIDE
L6             2 S NAPHTALIMIDE

=> s l3 and isoquinoline
         15940 ISOQUINOLINE
          2812 ISOQUINOLINES
         16902 ISOQUINOLINE
                (ISOQUINOLINE OR ISOQUINOLINES)
L7            28 L3 AND ISOQUINOLINE

=> d l7 1-27 iall

L7   ANSWER 1 OF 28  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:695950  CAPLUS
DOCUMENT NUMBER:          137:232561
ENTRY DATE:               Entered STN:  13 Sep 2002
TITLE:                    Glutarimide derivatives (thalidomide analogs and
                          homologs) with antiangiogenic and TNF-α
                          inhibitory activity, useful as therapeutic agents in
                          anticancer therapy
INVENTOR(S):              Fernandez Brana, Miguel; Anorbe Diaz, Loreto;
                          Dominguez Martin, Gema
PATENT ASSIGNEE(S):       Fundacion Universitaria San Pablo Ceu, Spain
SOURCE:                   PCT Int. Appl., 38 pp.
```

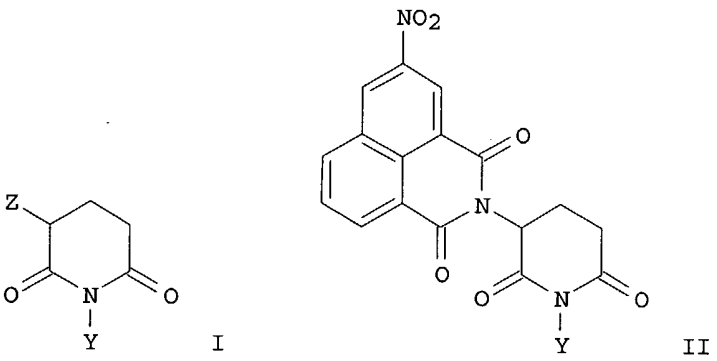
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
INT. PATENT CLASSIF.:
MAIN: C07D211-88
SECONDARY: A61K031-4412; A61P035-00; C07D401-04; C07D401-14; C07D401-12
CLASSIFICATION: 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070480	A1	20020912	WO 2002-ES92	20020301
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
ES 2172474	A1	20020916	ES 2001-488	20010301
ES 2172474	B1	20040116		

PRIORITY APPLN. INFO.: ES 2001-488 A 20010301
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002070480	ICM	C07D211-88
	ICS	A61K031-4412; A61P035-00; C07D401-04; C07D401-14; C07D401-12

OTHER SOURCE(S): MARPAT 137:232561
GRAPHIC IMAGE:



ABSTRACT:
The invention relates to novel glutarimide derivs. I and their dimeric homologs I-Q-I [wherein Z can be an imide or a bis-imide of various types; and Y and Q can be different types of atoms, chains, or organic groups]. The compds. can be considered to be homologs of thalidomide. The compds. are characterized (no data) by their concomitant antiangiogenic activity toward solid tumors, and by their inhibiting action toward alpha tumor necrosis factor (TNF-α). The compds. are prepared by general imide synthesis methods. Various salts, prodrugs of salts, and medicaments are obtained from the compds., for use in anti-cancer coadjuvant therapy using any clin. available means. Synthetic examples cover preparation of 14 compds. I and 7 intermediates. For instance, imidation of 3-nitro-1,8-naphthalic anhydride with L-glutamic acid in pyridine, followed by treatment with acetic anhydride, gave the corresponding imido-substituted anhydride, namely 2-(2,6-dioxotetrahydropyran-3-yl)-5-nitro-2H-benzo[de] ***isoquinoline*** -1,3-dione, in 78% yield. Ammonolysis of the anhydride and acidification gave a ring-opened acid amide (75%), which was cyclized by heating at 250° to give the invention diimide II (Y = H) in 30% yield.

Alternatively, aminolysis of the anhydride intermediate with H2NCH2CH2NMe2 and cyclization gave 37% II (Y = CH2CH2NMe2).

SUPPL. TERM: glutarimide thalidomide homolog prepn antiangiogenic TNF alpha inhibitor anticancer; tumor necrosis factor angiogenesis inhibitor cancer therapy naphthalimido glutarimide

INDEX TERM: Tumor necrosis factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of glutarimide derivs. (thalidomide analogs and homologs) with antiangiogenic and TNF-α inhibitory activity for anticancer therapy)

INDEX TERM: Angiogenesis inhibitors
Antitumor agents
(preparation of glutarimide derivs. (thalidomide analogs and homologs) with antiangiogenic and TNF-α inhibitory activity for anticancer therapy)

INDEX TERM: Neoplasm
(treatment of; preparation of glutarimide derivs. (thalidomide analogs and homologs) with antiangiogenic and TNF-α inhibitory activity for anticancer therapy)

INDEX TERM: 458151-26-3P, 2-(2,6-Dioxopiperidin-3-yl)-5-nitro-2H-benzo[de]**isoquinoline**-1,3-dione 458151-30-9P, 3-(2,5-Dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)piperidine-2,6-dione 458151-34-3P, 2-(2,6-Dioxopiperidin-3-yl)benzo[f]isoindole-1,3-dione **458151-38-7P**, 5-Amino-2-(2,6-dioxopiperidin-3-yl)-2H-benzo[de]**isoquinoline**-1,3-dione 458151-42-3P, 2,6-Bis(2,6-dioxopiperidin-3-yl)pyrrolo[3,4-f]isoindole-1,3,5,7-tetraone 458151-48-9P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]isoindol-1,3-dione hydrochloride 458151-54-7P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]-2H-benzo[de]**isoquinoline**-1,3-dione hydrochloride 458151-58-1P, 1-[2-(Dimethylamino)ethyl]-3-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)piperidine-2,6-dione hydrochloride 458151-62-7P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]benzo[f]isoindole-1,3-dione hydrochloride 458151-66-1P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]benzo[e]isoindole-1,3-dione hydrochloride 458151-70-7P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]-5-nitro-2H-benzo[de]**isoquinoline**-1,3-dione hydrochloride 458151-74-1P, 2,6-Bis[1-[2-(dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]pyrrolo[3,4-f]isoindole-1,3,5,7-tetraone dihydrochloride 458151-77-4P, N,N-Bis[2-[3-(1,3-dioxo-1,3-dihydroisoindol-2-yl)-2,6-dioxopiperidin-1-yl]ethyl]methylamine hydrochloride 458151-84-3P, N,N-Bis[3-[3-(1,3-dioxo-1,3-dihydroisoindol-2-yl)-2,6-dioxopiperidin-1-yl]propyl]methylamine hydrochloride 458151-88-7P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]isoindol-1,3-dione 458151-92-3P, 1-[2-(Dimethylamino)ethyl]-3-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)piperidine-2,6-dione 458151-96-7P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]benzo[e]isoindole-1,3-dione 458152-00-6P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]benzo[f]isoindole-1,3-dione 458152-03-9P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]-2H-benzo[de]**isoquinoline**-1,3-dione 458152-07-3P, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]-5-nitro-2H-benzo[de]**isoquinoline**-1,3-dione **458152-12-0P**, 2-[1-[2-(Dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]-5-amino-2H-benzo[de]

isoquinoline-1,3-dione 458152-20-0P, 2,6-Bis[1-[2-(dimethylamino)ethyl]-2,6-dioxopiperidin-3-yl]pyrrolo[3,4-f]isoindole-1,3,5,7-tetraone 458152-24-4P, N,N-Bis[2-[3-(1,3-dioxo-1,3-dihydroisoindol-2-yl)-2,6-dioxopiperidin-1-yl]ethyl]methylamine 458152-28-8P, N,N-Bis[2-[3-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)-2,6-dioxopiperidin-1-yl]ethyl]methylamine 458152-32-4P, N,N-Bis[2-[3-(1,2-naphthalimido)-2,6-dioxopiperidin-1-yl]ethyl]methylamine 458152-35-7P, N,N-Bis[2-[3-(2,3-naphthalimido)-2,6-dioxopiperidin-1-yl]ethyl]methylamine 458152-38-0P, N,N-Bis[2-[3-(1,8-naphthalimido)-2,6-dioxopiperidin-1-yl]ethyl]methylamine 458152-42-6P, N,N-Bis[2-[3-(3-nitro-1,8-naphthalimido)-2,6-dioxopiperidin-1-yl]ethyl]methylamine **458152-46-0P**, N,N-Bis[2-[3-(3-amino-1,8-naphthalimido)-2,6-dioxopiperidin-1-yl]ethyl]methylamine
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of glutarimide derivs. (thalidomide analogs and homologs) with antiangiogenic and TNF-α inhibitory activity for anticancer therapy)

INDEX TERM: 50-35-1DP, Thalidomide, homologs and derivs. 1121-89-7DP, Glutarimide, derivs.
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidates; preparation of glutarimide derivs. (thalidomide analogs and homologs) with antiangiogenic and TNF-α inhibitory activity for anticancer therapy)

INDEX TERM: 458150-90-8P, 2-(2,6-Dioxotetrahydropyran-3-yl)benzo[de]**isoquinoline**-1,3-dione 458150-94-2P, 1-(2,6-Dioxotetrahydropyran-3-yl)-3,4-diphenylpyrrole-2,5-dione 458150-99-7P 458151-04-7P, 2-(2,6-Dioxotetrahydropyran-3-yl)benzo[f]isoindole-1,3-dione 458151-10-5P, 2-(2,6-Dioxotetrahydropyran-3-yl)benzo[e]isoindole-1,3-dione 458151-16-1P, 4-Carbamoyl-2-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)butyric acid 458151-21-8P, 4-Carbamoyl-2-(5-nitro-1,3-dioxo-1,3-dihydrobenzo[de]isoquinolin-2-yl)butyric acid
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of glutarimide derivs. (thalidomide analogs and homologs) with antiangiogenic and TNF-α inhibitory activity for anticancer therapy)

INDEX TERM: 56-86-0, L-Glutamic acid, reactions 81-84-5, Naphthalic anhydride 89-32-7, 1,2,4,5-Benzenetetracarboxylic dianhydride 105-83-9, N-(3-Aminopropyl)-N-methyl-1,3-propanediamine 108-00-9, N,N-Dimethylethylenediamine 716-39-2, 2,3-Naphthalic anhydride 3027-38-1, 3-Nitro-1,8-naphthalic anhydride 3343-28-0, 2-(2,6-Dioxotetrahydropyran-3-yl)isoindol-1,3-dione 4097-88-5, N-(2-Aminoethyl)-N-methylethylenediamine 4808-48-4, Diphenylmaleic anhydride 5343-99-7, 1,2-Naphthalic anhydride 24666-56-6, 3-Amino-2,6-piperidinedione hydrochloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(precursor; preparation of glutarimide derivs. (thalidomide analogs and homologs) with antiangiogenic and TNF-α inhibitory activity for anticancer therapy)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Cegene Corp; EP 1004580 A 2000 CAPLUS
(2) Chemie Gruenenthal; GB 1075420 A 1967
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L7 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:532512 CAPLUS
DOCUMENT NUMBER: 138:214841
ENTRY DATE: Entered STN: 17 Jul 2002
TITLE: Synthesis and antitumour activity of new dendritic polyamines-(imide-DNA-intercalator) conjugates: potent Lck inhibitors
AUTHOR(S): Brana, Miguel F.; Dominguez, Gema; Saez, Beatriz; Romerdahl, Cynthia; Robinson, Simmon; Barlozzari, Teresa
CORPORATE SOURCE: Facultad de Ciencias Experimentales y Tecnicas, Departamento de Quimica Organica y Farmaceutica, Universidad San Pablo-CEU, Boadilla del Monte, Madrid, 28668, Spain
SOURCE: European Journal of Medicinal Chemistry (2002), 37(7), 541-551
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-3 (Pharmacology)
OTHER SOURCE(S): CASREACT 138:214841
ABSTRACT:
A series of dendritic polyamines-(imide-DNA-intercalators) conjugates with different connectivity in their basic chain were synthesized and evaluated as antitumor compds. Although their antiproliferative activity against HT-29 was not significant, conjugates 13 and 16 showed a promising profile as inhibitors of Lck.

SUPPL. TERM: antitumor design amonafide elinafide deriv monointercalator bisintercalator human
INDEX TERM: Structure-activity relationship
(antitumor; synthesis and antitumor activity of new dendritic polyamines-(imide-DNA-intercalator) conjugates)
INDEX TERM: Antitumor agents
Drug design
Drug screening
Human
(synthesis and antitumor activity of new dendritic polyamines-(imide-DNA-intercalator) conjugates)
INDEX TERM: 162265-51-2P 412008-02-7P 412008-03-8P 412008-04-9P **412008-05-0P** 412008-06-1P 412008-07-2P 412008-08-3P **412008-09-4P** 412008-10-7P 500904-27-8P 500904-28-9P 500904-29-0P 500904-30-3P 500904-31-4P
ROLE: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and antitumor activity of new dendritic polyamines-(imide-DNA-intercalator) conjugates)
INDEX TERM: 500904-32-5P
ROLE: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and antitumor activity of new dendritic polyamines-(imide-DNA-intercalator) conjugates)

INDEX TERM: 57260-73-8P 220170-79-6P 412008-01-6P 500904-24-5P
500904-25-6P 500904-26-7P
ROLE: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of new dendritic polyamines-(imide-DNA-intercalator) conjugates)

INDEX TERM: 81-83-4, 1H-Benz[de]**isoquinoline**-1,3(2H)-dione
81-84-5, 1,8-Naphthalenedicarboxylic anhydride 96-33-3, Methyl acrylate 3027-38-1, 3-Nitro-1,8-naphthalic anhydride 4808-48-4, 2,3-Diphenylmaleic anhydride 23204-38-8 **23204-40-2** 24424-99-5, Di-tert-butyldicarbonate 31295-36-0 66266-36-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and antitumor activity of new dendritic polyamines-(imide-DNA-intercalator) conjugates)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

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L7 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:780664 CAPLUS
DOCUMENT NUMBER: 135:313609
ENTRY DATE: Entered STN: 26 Oct 2001
TITLE: Naphthalimide compositions for the treatment of a host with a cellular proliferative disease

INVENTOR(S): Brown, Dennis M.
PATENT ASSIGNEE(S): Chemgenex Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-00
CLASSIFICATION: 1-6 (Pharmacology)
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078705	A2	20011025	WO 2001-US12169	20010412
WO 2001078705	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002025916	A1	20020228	US 2001-834177	20010412
US 6630173	B2	20031007		
EP 1274458	A2	20030115	EP 2001-926985	20010412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003530431	T2	20031014	JP 2001-576006	20010412
US 2004047918	A1	20040311	US 2003-631106	20030731

PRIORITY APPLN. INFO.:

US 2000-197103P	P	20000412
US 2001-810527	A2	20010315
US 2001-834177	A3	20010412
WO 2001-US12169	W	20010412

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001078705	ICM	A61K031-00
US 2002025916	ECLA	A61K031/47; A61K031/505; A61K031/70R5; A61K045/06
US 2004047918	ECLA	A61K031/47; A61K031/4745; A61K031/475; A61K031/505; A61K031/513; A61K031/55; A61K031/70; A61K031/7048; A61K031/7076; A61K033/24; A61K045/06; A61K045/06

ABSTRACT:
A method of treatment of a host with a cellular proliferative disease, comprising contacting the host with a naphthalimide and an antiproliferative agent, each in an amount sufficient to modulate said cellular proliferative disease, is described (Markush structures given). In some embodiments, the naphthalimide comprises amonafide (5-amino-2-[2-(dimethylamine)ethyl]-1H-benz[de-]**isoquinoline**-1,3-(2H)-dione). Antiproliferative agents of the invention comprise alkylating agents, intercalating agents, metal coordination complexes, pyrimidine nucleosides, purine nucleosides, inhibitors of nucleic acid associated enzymes and proteins, and agents affecting structural proteins and cytoplasmic enzymes. The invention comprises the described methods as well as compns. comprising a naphthalimide and an antiproliferative agent. The antiproliferative activity of cisplatin (4 mg/kg) was enhanced by the use of chemopotentiator amonafide (50 mg/kg), in that a more than additive effect was observed when both compds. were used to treat the murine fibrosarcoma-bearing mice in comparison to the use of cisplatin alone or amonafide alone.

SUPPL. TERM: naphthalimide compn cell proliferative disease; synergistic antiproliferative agent cisplatin amonafide

INDEX TERM: Intercalation
(agents; naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: Coordination compounds
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metal; naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: Alkylating agents, biological
(naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: Purine nucleosides
Pyrimidine nucleosides
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: Nucleic acids
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: Proliferation inhibition
(proliferation inhibitors; naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: Disease, animal
(proliferative; naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: Antitumor agents
(synergistic; naphthalimide compns. for treatment of host with cellular proliferative disease)
INDEX TERM: 51-21-8, 5-Fluorouracil 64-86-8, Colchicine 81-83-4D, Naphthalimide, derivs. 458-37-7, Curcumine 865-21-4, Vinblastine 15663-27-1, Cisplatin 20554-84-1, Parthenolide 26833-87-4, Homoharringtonine 33069-62-4, Paclitaxel 33419-42-0, Etoposide **69408-81-7**, Amonafide
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(naphthalimide compns. for treatment of host with cellular proliferative disease)

L7 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:227437 CAPLUS
DOCUMENT NUMBER: 132:251289
ENTRY DATE: Entered STN: 07 Apr 2000
TITLE: Preparation of ecteinascidin 743 analogs for pharmaceutical use as antitumor agents
INVENTOR(S): Corey, Elias J.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A01N043-58
SECONDARY: C07D241-36
CLASSIFICATION: 31-6 (Alkaloids)
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018233	A1	20000406	WO 1999-US22405	19990930
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6124292	A	20000926	US 1998-165892	19980930
CA 2345297	AA	20000406	CA 1999-2345297	19990930
AU 9961650	A1	20000417	AU 1999-61650	19990930
AU 765439	B2	20030918		
EP 1117297	A1	20010725	EP 1999-948484	19990930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525296	T2	20020813	JP 2000-571761	19990930
NZ 510734	A	20031031	NZ 1999-510734	19990930
US 6348467	B1	20020219	US 2000-510315	20000222
US 6569859	B1	20030527	US 2002-77700	20020214

PRIORITY APPLN. INFO.:

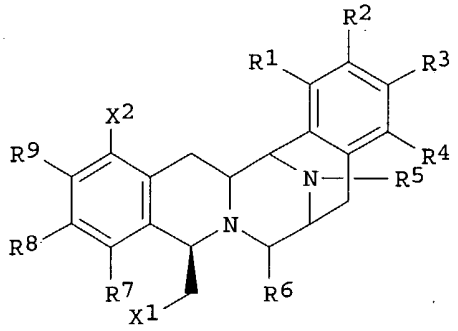
US 1998-165892	A	19980930
WO 1999-US22405	W	19990930
US 2000-510315	A1	20000222

PATENT CLASSIFICATION CODES:

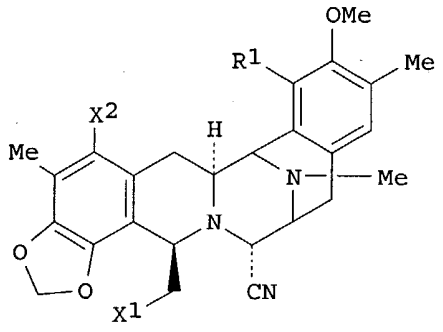
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000018233	ICM	A01N043-58
	ICS	C07D241-36

OTHER SOURCE(S): MARPAT 132:251289

GRAPHIC IMAGE:



I



II

ABSTRACT:

Ecteinascidin 743 analogs I [R1, R2, R3, R4, R5, R6, R7, R8, R9 = H, OH, SH, NO2, NH2, CHO, CO2H, alkyloxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, halogen, alkyl, alkenyl, alkynyl, aryl, etc.; X1, X2 = H, OH, SH, NO2, NH2, CHO, CO2H, alkyloxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, halogen, phthalimido, etc.] were prepared for use as anticancer agents. Thus, ecteinascidin 743 analogs II (R1 = OH, X1 = phthalimido, X2 = AcO) was prepared in a series of synthetic steps via coupling of phthalimide with II (R1 = MeOCH2O, X1 = OH, X2 = CH2:CHCH2O). The prepared compds. were tested for antitumor activity against a variety of cancer cell lines, such as lung, colon, prostate and melanoma.

SUPPL. TERM: ecteinascidin analog prepn antitumor agent

INDEX TERM: Antitumor agents
(preparation of ecteinascidin 743 analogs for pharmaceutical use as antitumor agents)

INDEX TERM: 236743-64-9P 236743-94-5P 236743-97-8P 236743-98-9P
236744-03-9P 236744-08-4P 237756-93-3P 262842-12-6P
262842-13-7P 262842-14-8P 262842-15-9P 262842-19-3P
262842-23-9P 262842-40-0P 262842-43-3P 262842-44-4P
262842-46-6P 262842-47-7P 262842-53-5P 262842-54-6P
262842-56-8P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of ecteinascidin 743 analogs for pharmaceutical use as antitumor agents)

INDEX TERM: 114899-77-3DP, Ecteinascidin 743, analogs 236743-90-1P
237756-72-8P 237756-74-0P 237756-75-1P 237756-77-3P
237756-78-4P 237756-80-8P 237756-81-9P 237756-83-1P
237756-84-2P 237756-91-1P 262842-16-0P 262842-17-1P
262842-18-2P 262842-20-6P 262842-21-7P 262842-22-8P
262842-24-0P 262842-25-1P **262842-26-2P**
262842-27-3P 262842-28-4P 262842-29-5P 262842-30-8P
262842-31-9P 262842-32-0P 262842-33-1P 262842-34-2P
262842-35-3P 262842-36-4P 262842-37-5P 262842-38-6P
262842-39-7P 262842-41-1P 262842-42-2P 262842-45-5P
262842-48-8P 262842-49-9P 262842-50-2P 262842-51-3P
262842-52-4P 262842-55-7P 262842-57-9P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ecteinascidin 743 analogs for pharmaceutical use as antitumor agents)

INDEX TERM: 75-03-6, Iodoethane 75-30-9, 2-Iodopropane 77-78-1, Dimethyl sulfate 79-09-4, Propanoic acid, reactions
81-83-4, 1H-Benz[de]**isoquinoline**-1,3(2H)-dione
85-41-6, Phthalimide 89-40-7 91-13-4 98-88-4, Benzoyl chloride 103-71-9, Phenyl isocyanate, reactions
103-82-2, Benzeneacetic acid, reactions 106-31-0, Butanoic acid anhydride 106-95-6, Allyl bromide, reactions
116-11-0, 2-Methoxy-1-propene 123-56-8, 2,5-Pyrrolidinedione 127-17-3, Pyruvic acid, reactions
156-38-7, 4-Hydroxybenzeneacetic acid 501-52-0, Benzenepropanoic acid 543-24-8, N-Acetylglycine 603-62-3
625-45-6, Methoxyacetic acid 4379-50-4, 1H-Benz[e]isoindole-1,3(2H)-dione 4379-54-8, 1H-Benz[f]isoindole-1,3(2H)-dione 4720-86-9 6941-75-9
7506-66-3 15997-89-4 18303-04-3 38177-33-2, EJM-III
124C 66266-36-2 160037-32-1 182201-59-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of ecteinascidin 743 analogs for pharmaceutical

use as antitumor agents)
INDEX TERM: 114774-40-2P 236744-11-9P 262842-58-0P 262842-59-1P
262842-60-4P 262842-61-5P 262842-62-6P 262842-63-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation of ecteinascidin 743 analogs for pharmaceutical
use as antitumor agents)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD.
REFERENCE(S): (1) Corey; J Am Chem Soc 1996, V118(38), P9202 CAPLUS
(2) Fukuyama; J Am Chem Soc 1982, V104(18), P4957 CAPLUS
(3) Fukuyama; J Am Chem Soc 1990, V112(9), P3712 CAPLUS
(4) Lown; Biochemistry 1982, V21(3), P419 CAPLUS
(5) Sakai; J Am Chem Soc 1996, V118(38), P9017 CAPLUS

L7 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:34858 CAPLUS
DOCUMENT NUMBER: 132:93221
ENTRY DATE: Entered STN: 14 Jan 2000
TITLE: Preparation of naphthalimidobenzamide derivatives as
antitumor agents
INVENTOR(S): Noguchi, Kazuharu; Wakida, Motoji; Suzuki, Kenji;
Yamada, Yuji; Asao, Tetsuji
PATENT ASSIGNEE(S): Taiho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
INT. PATENT CLASSIF.:
MAIN: C07D221-14
SECONDARY: C07D401-12; C07D401-14; A61K031-47; A61K031-495;
A61K031-535
CLASSIFICATION: 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001672	A1	20000113	WO 1999-JP3574	19990702
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2300069	AA	20000113	CA 1999-2300069	19990702
AU 9943963	A1	20000124	AU 1999-43963	19990702
AU 727591	B2	20001214		
EP 1020446	A1	20000719	EP 1999-926895	19990702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 3357662	B2	20021216	JP 2000-558077	19990702
US 6300331	B1	20011009	US 2000-508044	20000303
PRIORITY APPLN. INFO.:			JP 1998-189078 A	19980703
			WO 1999-JP3574 W	19990702

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000001672	ICM	C07D221-14
	ICS	C07D401-12; C07D401-14; A61K031-47; A61K031-495; A61K031-535

OTHER SOURCE(S): MARPAT 132:93221
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
2-(3-Carbamoylphenyl)-1H-benz[de]**isoquinoline**-1,3(2H)-dione derivs. represented by general formula (I) or salts thereof (wherein R1 is hydrogen,NO2, OH, NH2, halo, cyano, CO2H, CONH2, ureido, alkyl, trihaloalkyl, alkoxy, etc.; Y is hydrogen or -CON(R4)-A2-X2; R2 and R4 are each independently hydrogen or alkyl; A1 and A2 are each independently linear or branched alkylene which may be interrupted by N(R3), O, S, CONH, NHCO, S(O), or SO2 (wherein R3 is hydrogen or the like); X1 is optionally substituted aryl, heteroaryl, aryldicarbonylimino, heteroaryldicarbonylimino, arylamino, heteroarylamino, arylcarbonylamino, etc.; and X2 is H, optionally substituted aryl, heterocyclyl, aryldicarbonylimino, heteroaryldicarbonylimino, arylamino, heteroarylamino, arylcarbamoyl, etc.; m = 1-3), which exhibit high affinity for DNA, are prepared Thus, a suspension of 711 mg 1-[N-[2-[(2-aminoethyl)amino]ethyl]carbamoyl]-3-(3-nitro-1,8-naphthalimido)-5-[N-(2-piperidinoethyl)carbamoyl]benzene hydrochloride, 0.5 mL Et3N, and 243 mg 3-nitro-1,8-naphthalic anhydride in 4 mL DMF was stirred at 60° for 30 min to give 72.2% title compound (II.HCl). II.HCl in vivo inhibited the proliferation of human melanoma LOX, human pancreatic cancer PAN, human breast cancer MX1, and human stomach cancer AZ521 cells transplanted s.c. in nude mice by 96.2, 59.8, 71.8, and 79.5%, resp.

SUPPL. TERM: naphthalimidobenzamide prepn antitumor; carbamoylphenylbenzisoquinolinedione prepn antitumor; benzisoquinolinedione carbamoylphenyl prepn antitumor

INDEX TERM: Antitumor agents
(preparation of naphthalimidobenzamide derivs. as antitumor agents)

INDEX TERM:
254451-70-2P 254451-72-4P 254451-74-6P 254451-75-7P
254451-76-8P 254451-77-9P 254451-78-0P 254451-79-1P
254451-80-4P 254451-81-5P 254451-82-6P 254451-83-7P
254451-84-8P 254451-85-9P 254451-86-0P 254451-87-1P
254451-88-2P 254451-89-3P 254451-90-6P 254451-91-7P
254451-92-8P 254451-93-9P 254451-94-0P 254451-95-1P
254451-96-2P 254451-97-3P 254451-98-4P 254451-99-5P
254452-00-1P 254452-01-2P 254452-02-3P 254452-03-4P
254452-04-5P 254452-05-6P 254452-06-7P 254452-07-8P
254452-08-9P **254452-09-0P** 254452-10-3P
254452-11-4P 254452-12-5P 254452-13-6P 254452-14-7P
254452-15-8P 254452-16-9P 254452-17-0P 254452-18-1P
254452-19-2P 254452-20-5P 254452-21-6P 254452-22-7P
254452-23-8P 254452-24-9P 254452-25-0P 254452-26-1P
254452-27-2P 254452-28-3P 254452-29-4P 254452-30-7P
254452-58-9P 254453-06-0P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphthalimidobenzamide derivs. as antitumor agents)

INDEX TERM: 60-34-4, Methylhydrazine 81-84-5, 1,8-Naphthalic anhydride 99-05-8, 3-Aminobenzoic acid 99-31-0, 5-Aminoisophthalic acid 244-63-3, Norharman 486-74-8, 4-Quinolinecarboxylic acid 716-39-2, 2,3-Naphthalic anhydride 879-65-2, 2-Quinoxalinecarboxylic acid 3027-38-1, 3-Nitro-1,8-naphthalic anhydride 4053-08-1, 4-Chloro-1,8-naphthalic anhydride 5105-78-2, 4-((Benzyloxycarbonyl)amino)butanoic acid 6480-68-8, 3-Quinolinecarboxylic acid 13531-52-7, N-(2-Aminoethyl)-1,3-propanediamine 16136-58-6, 1-Methyl-2-indolecarboxylic acid 22509-74-6, N-Ethoxycarbonylphthalimide 26628-22-8, Sodium azide

65361-31-1 254452-35-2 254452-43-2 254452-59-0
254452-60-3, 4-Nitro-1-methyl-2-(trichloromethyl)pyrrole
254452-61-4 254452-62-5
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of naphthalimidobenzamide derivs. as antitumor agents)

INDEX TERM: 530-62-1P, N,N'-Carbonyldiimidazole 118970-65-3P
118970-66-4P 118970-67-5P 254452-31-8P 254452-32-9P
254452-33-0P 254452-34-1P 254452-36-3P 254452-37-4P
254452-38-5P 254452-39-6P 254452-40-9P 254452-41-0P
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254452-55-6P 254452-56-7P 254452-57-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of naphthalimidobenzamide derivs. as antitumor agents)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Du Pont Merk Pharm Co; JP 06506229 A
(2) Du Pont Merk Pharm Co; JP 07501822 A
(3) Du Pont Merk Pharm Co; EP 506008 A CAPLUS
(4) Du Pont Merk Pharm Co; US 5206249 A CAPLUS
(5) Du Pont Merk Pharm Co; US 5329048 A CAPLUS
(6) Du Pont Merk Pharm Co; EP 577753 A CAPLUS
(7) Du Pont Merk Pharm Co; EP 618901 A CAPLUS
(8) Du Pont Merk Pharm Co; AU 9332415 A CAPLUS
(9) Du Pont Merk Pharm Co; WO 9217453 A1 1992 CAPLUS
(10) Du Pont Merk Pharm Co; WO 9312092 A1 1993 CAPLUS
(11) Knoll Ag; JP 05503509 A
(12) Knoll Ag; DE 3942280 A CAPLUS
(13) Knoll Ag; EP 505400 A CAPLUS
(14) Knoll Ag; WO 919850 A1 1991
(15) Warner-Lambert Co; US 4499266 A CAPLUS
(16) Warner-Lambert Co; US 4594346 A CAPLUS
(17) Warner-Lambert Co; US 4614820 A CAPLUS
(18) Warner-Lambert Co; US 4665071 A CAPLUS
(19) Warner-Lambert Co; JP 601166 A
(20) Warner-Lambert Co; EP 125439 A 1984 CAPLUS

L7 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:406187 CAPLUS
DOCUMENT NUMBER: 129:55412
ENTRY DATE: Entered STN: 02 Jul 1998
TITLE: Pyrrolo- and thiophenoperylenedicarboximide strongly fluorescent heterocycles, their preparation and their use
INVENTOR(S): Langhals, Heinz; Feiler, Leonhard
PATENT ASSIGNEE(S): Langhals, Heinz, Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: C09B005-62
SECONDARY: C09K011-06; D06P001-22; C09D017-00; C09D011-00; C09D005-22; C08J003-20; D21H021-28; G03G009-09; G01N021-64; G01N021-76; G01N023-223
ADDITIONAL: D06P003-32; D06P003-30; D06P003-60; D06P003-14; C09D011-02; C09D011-16; C07D221-14; C07D471-06
CLASSIFICATION: 41-5 (Dyes, Organic Pigments, Fluorescent Brighteners, and Photographic Sensitizers)
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19651712	A1	19980618	DE 1996-19651712	19961212
PRIORITY APPLN. INFO.:			DE 1996-19651712	19961212

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 19651712	ICM	C09B005-62
	ICS	C09K011-06; D06P001-22; C09D017-00; C09D011-00; C09D005-22; C08J003-20; D21H021-28; G03G009-09; G01N021-64; G01N021-76; G01N023-223
	ICA	D06P003-32; D06P003-30; D06P003-60; D06P003-14; C09D011-02; C09D011-16; C07D221-14; C07D471-06

OTHER SOURCE(S): MARPAT 129:55412

ABSTRACT:
2H,3H,4H-isoquinolino[5',6':3,4][4,4a,5-bc]naphtho[3,2,1,1a,8-def]carbazole-2,4-diones substituted at the 3, 6, and 12 positions and 2H,3H,4H-benzo[b]thiopheno[2',3',3a',4',5':4,4a,10,10a,5]anthra[1,2,8a,9,9a-def] ***isoquinoline*** -2,4-diones substituted at the 3-position were obtained by reductive cyclization of the appropriate 1-nitroperylene-3,4-dicarboximide and were useful as fluorescent materials, such as dyes. In an example, fluorescent orange 3-(1-hexylheptyl)-2H,3H,4H-isoquinolino[5',6':3,4][4,4a,5-bc]naphtho[3,2,1,1a,8-def]carbazole-2,4-dione was obtained by refluxing N-(1-hexylheptyl)-1-nitroperylene-3,4-dicarboximide with Et3PO3.

SUPPL. TERM: isoquinolinonaphthocarbazoledione fluorescent dye prodn; benzothiophenoanthraqisoquinolinedione fluorescent dye prodn; fluorescent dye perylenedicarboximide deriv prodn

INDEX TERM: Fluorescent dyes
(production of fluorescent perylenedicarboximide dye derivs.)

INDEX TERM: 183017-43-8P
ROLE: IMF (Industrial manufacture); RCT (Reactant); TEM (Technical or engineered material use); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(orange dye; production of fluorescent perylenedicarboximide dye derivs.)

INDEX TERM: 183017-47-2P 183017-48-3P 183017-49-4P 183017-50-7P 183017-51-8P
ROLE: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(orange dye; production of fluorescent perylenedicarboximide dye derivs.)

INDEX TERM: 183017-45-0P
ROLE: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(orange red dye; production of fluorescent perylenedicarboximide dye derivs.)

INDEX TERM: 183017-44-9P 183017-46-1P
ROLE: IMF (Industrial manufacture); RCT (Reactant); TEM (Technical or engineered material use); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(red dye; production of fluorescent perylenedicarboximide dye derivs.)

INDEX TERM: 183017-52-9P
ROLE: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(red dye; production of fluorescent perylenedicarboximide dye derivs.)

INDEX TERM: 122-52-1, Triethyl phosphite
ROLE: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(starting material and reductant; production of fluorescent

perylenedicarboximide dye derivs.)

INDEX TERM: 74-88-4, Methyl iodide, reactions 75-36-5, Acetyl chloride 98-88-4, Benzoyl chloride 100-44-7, Benzyl chloride, reactions 165261-40-5, N-(1-Hexylheptyl)-1-nitroperylene-3,4-dicarboximide 165261-41-6, N-(2,5-Di-tert-butylphenyl)-1-nitroperylene-3,4-dicarboximide 165261-43-8, N-(1-Hexylheptyl)-1,6-dinitroperylene-3,4-dicarboximide
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(starting material; production of fluorescent perylenedicarboximide dye derivs.)

INDEX TERM: 183017-53-0P **183017-54-1P**
ROLE: BYP (Byproduct); PREP (Preparation)
(violet byproduct; production of fluorescent perylenedicarboximide dye derivs.)

L7 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:268358 CAPLUS
DOCUMENT NUMBER: 128:317269
ENTRY DATE: Entered STN: 11 May 1998
TITLE: Benzoisoquinolinedione neurotrophin antagonist compositions and therapeutic use
INVENTOR(S): Tehim, Ashok; Chen, Xiannong
PATENT ASSIGNEE(S): Allelix Biopharmaceuticals Inc., Can.; Tehim, Ashok; Chen, Xiannong
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-47
SECONDARY: C07D221-14; C07D401-04; C07D401-06
CLASSIFICATION: 1-11 (Pharmacology)
Section cross-reference(s): 27, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817278	A1	19980430	WO 1997-CA779	19971020
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2268450	AA	19980430	CA 1997-2268450	19971020
AU 9746968	A1	19980515	AU 1997-46968	19971020
AU 728523	B2	20010111		
EP 930883	A1	19990728	EP 1997-909098	19971020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 335291	A	20010223	NZ 1997-335291	19971020
JP 2001503397	T2	20010313	JP 1998-518756	19971020
BR 9712424	A	20011120	BR 1997-12424	19971020
MX 9903637	A	20000531	MX 1999-3637	19990420
US 2002169182	A1	20021114	US 2001-758917	20010111

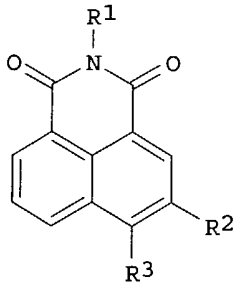
PRIORITY APPLN. INFO.:		
GB 1996-21902	A	19961021
GB 1997-10904	A	19970527
WO 1997-CA779	W	19971020
US 1999-292458	B1	19990415
US 1999-440505	B1	19991115
US 2000-592015	A1	20000612

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9817278	ICM	A61K031-47
	ICS	C07D221-14; C07D401-04; C07D401-06
US 2002169182	ECLA	A61K031/47N; C07D221/14A; C07D401/04; C07D401/06; C07D405/06

OTHER SOURCE(S): MARPAT 128:317269

GRAPHIC IMAGE:



I

ABSTRACT:
Pharmaceutical compns. comprising I (R1 = alkyl, aryl-lower alkyl, heterocyclyl-lower alkyl, etc.; R2, R3 = H, NO2, halo, di(lower alkyl)amino, cyano, etc.), or pharmaceutically acceptable salts or certain in vivo hydrolyzable esters or amides thereof, in an amount effective to inhibit neurotrophin-mediated activity, and a suitable carrier, are described. The compns. are useful for inhibiting undesirable neurotrophin-mediated activity, e.g. the neurite outgrowth that occurs in some neurodegenerative disease states. N-[5-nitro-1H-benz[de]**isoquinoline**-1,3(2H)-dione]-2-aminoethanol (II) was prepared from 3-nitro-1,8-naphthalic anhydride and 2-hydroxyethylhydrazine. II was tested for ability to inhibit neurite outgrowth, as well as in an animal model of neuropathic pain. Compds. of the invention were also tested for ability to inhibit NGF binding to P75 and TrkA.

SUPPL. TERM: benzoisoquinolinedione neurotrophin antagonist neurite outgrowth inhibition; neurodegenerative disease benzoisoquinolinedione neurotrophin antagonist prepn; neuropathic pain benzoisoquinolinedione neurotrophin antagonist

INDEX TERM: Neurotrophic factor receptors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(TrkA; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Pain
Pain
Skin, disease
Skin, disease
(allodynia, tactile; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Analgesics
Drug delivery systems
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Neurotrophic factors
ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Neurotrophic factors
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(brain-derived; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Pain
(hyperalgesia, thermal; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Nerve
(neuron; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Pain
(neuropathic; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Axon
(outgrowth, inhibition; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: Nerve growth factor receptors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p75; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: 9061-61-4, NGF
ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: 79070-65-8P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

INDEX TERM: 2382-08-3 5450-40-8 5690-46-0 5690-46-0D, esters and amides 5810-79-7 6917-30-2D, esters and amides 15965-03-4 15965-03-4D, esters and amides 51411-04-2D, esters and amides 53497-34-0 53497-34-0D, esters and amides 66266-36-2 69408-78-2 74240-33-8 79070-65-8D, esters and amides 94887-57-7 100873-54-9
130001-49-9 162265-47-6 194610-48-5
206982-84-5 207107-62-8 207107-63-9 207107-64-0
207107-65-1 207107-66-2 207107-67-3 207107-68-4
207107-69-5 207107-70-8 207107-71-9 207107-72-0
207107-73-1 207107-74-2 207107-75-3 207107-76-4
207107-77-5 207107-78-6 207107-79-7 207107-80-0
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

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(3) Brana, M; JOURNAL OF ORGANIC CHEMISTRY 1996, V61(4), P1369 CAPLUS
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(6) Knoll Ag; DE 3707652 A 1988 CAPLUS
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L7 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:375288 CAPLUS
DOCUMENT NUMBER: 127:81360
ENTRY DATE: Entered STN: 16 Jun 1997
TITLE: Preparation of dibenz[de,h]**isoquinoline**-1,3-diones antitumor agents
INVENTOR(S): Alberts, David S.; Dorr, Robert T.; Remers, William A.; Sami, Salah M.
PATENT ASSIGNEE(S): Research Corporation Technologies, Inc., USA
SOURCE: U.S., 39 pp., Cont.-in-part of U.S. Ser. No. 943,634, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-435
SECONDARY: C07D221-18; C07D411-06; C07D413-06
US PATENT CLASSIF.: 514232800
CLASSIFICATION: 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5635506	A	19970603	US 1993-142283	19931118
WO 9406771	A1	19940331	WO 1993-US8640	19930913

W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.:

US 1990-543596	B1	19900626
US 1991-803314	B2	19911204
US 1992-943634	B2	19920911
WO 1993-US8640	W	19930913

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5635506	ICM	A61K031-435
	ICS	C07D221-18; C07D411-06; C07D413-06
	NCL	514232800

OTHER SOURCE(S): MARPAT 127:81360
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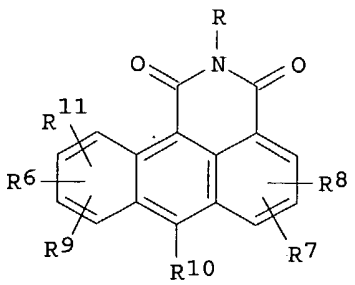

I

ABSTRACT:
Title compds. [I; R = Z1Z1NR12R13; R6,R8,R10 = H, halo, alkyl, alkoxy, etc.; R7,R9,R11 = H or alkyl; R9R11,R9R10,R7R10 = CH:CHCH:CH; R12,R13 = H or (un)substituted Ph; NR12R13 = heterocyclyl; Z1 = bond, alkylene, arylene; Z2 = bond; Z2R12 = atoms to form a heterocyclic ring] were prepared Thus, anthracene-1,9-dicarboxylic acid was treated with acetic anhydride and the product cyclocondensed with H2NCH2CH2NMe2 to give I (R = CH2CH2NMe2, R6-R11 = H). Data for biol. activity of I were given.

SUPPL. TERM: benzisoquinolinedione prepn antitumor

INDEX TERM: Antitumor agents
(dibenz[de,h]**isoquinoline**-1,3-diones)

INDEX TERM:

140917-67-5P	140917-68-6P	140917-69-7P	140917-70-0P
140917-71-1P	140917-72-2P	140917-73-3P	140917-74-4P
140917-75-5P	140917-76-6P	140917-77-7P	140917-78-8P
140917-79-9P	140917-80-2P	140917-81-3P	140917-82-4P
140917-83-5P	140917-84-6P	140917-85-7P	140917-86-8P
140917-87-9P	140917-88-0P	140917-89-1P	140917-90-4P
140917-91-5P	140917-92-6P	140917-93-7P	140917-95-9P
140917-96-0P	140917-97-1P	140917-98-2P	140917-99-3P
140918-00-9P	140918-01-0P	140918-02-1P	
140918-03-2P	140918-04-3P	140918-05-4P	
140918-06-5P	140918-07-6P	140918-08-7P	140918-09-8P
140918-10-1P	140918-11-2P	140918-12-3P	140918-13-4P
140918-14-5P	140918-15-6P	140918-16-7P	140918-17-8P
140918-18-9P	140918-19-0P	140918-20-3P	140918-21-4P
140918-22-5P	140918-23-6P	140918-24-7P	140918-25-8P
140918-26-9P	140918-27-0P	140918-28-1P	140918-29-2P
140918-30-5P	140918-31-6P	140918-32-7P	140918-33-8P
140937-11-7P	140937-12-8P	146516-60-1P	146516-63-4P
146516-64-5P	160554-73-4P	160554-75-6P	160554-76-7P
160554-77-8P	160554-78-9P	160554-79-0P	160554-80-3P
160554-81-4P	160554-82-5P	160554-83-6P	160554-84-7P
160554-85-8P	160554-86-9P	160554-87-0P	160554-88-1P
160554-89-2P	160554-90-5P	160554-91-6P	160554-92-7P
160554-93-8P	160554-94-9P	160554-95-0P	160554-96-1P
160554-97-2P	160554-98-3P	160554-99-4P	160555-00-0P
160555-01-1P	160555-02-2P	160555-23-7P	191799-96-9P
191799-97-0P			

ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dibenz[de,h]**isoquinoline**-1,3-diones antitumor agents)

INDEX TERM: 6929-82-4P, 10-Chloro-9-anthroic acid 22023-39-8P, 10-Methyl-9-anthroic acid
ROLE: BYP (Byproduct); PREP (Preparation)
(preparation of dibenz[de,h]**isoquinoline**-1,3-diones antitumor agents)

INDEX TERM: 99-98-9, N,N-Dimethyl-p-phenylenediamine 108-00-9, N,N-Dimethylethylenediamine 109-55-7, 3-Dimethylaminopropylamine 111-41-1 140-31-8, 1-Piperazineethanamine 610-48-0, 1-Methylanthracene 613-12-7, 2-Methylanthracene 613-13-8, 2-Aminoanthracene 716-53-0, 9-Chloroanthracene 779-02-2, 9-Methylanthracene 1564-64-3, 9-Bromoanthracene 2038-03-1, 4-(2-Aminoethyl)morpholine 2706-56-1, 2-(2-Aminoethyl)pyridine 3282-30-2, Trimethylacetyl chloride 3586-89-8, 1,2,3,4-Tetrahydro-7-nitroanthracene 3731-52-0, 3-Aminomethylpyridine 4025-37-0, 1-(2-Aminoethyl)aziridine 4985-70-0, 1-Chloroanthracene 4985-85-7, N-(3-Aminopropyl)diethanolamine 6789-94-2,

3-Amino-1-ethylpiperidine 7154-73-6, 1-(2-Aminoethyl)pyrrolidine 14381-66-9, 1,8-DiChloroanthracene 17135-78-3, 2-Chloroanthracene 21454-60-4, 2-Fluoroanthracene 22362-90-9, 1-Iodoanthracene 22362-94-3, 2-Iodoanthracene 27578-60-5, 1-Piperidineethanamine 37170-96-0, N-(9-Anthracenyl)acetamide 42298-28-2, 2-Methoxyanthracene 51384-67-9, Anthracene-1,9-dicarboxylic acid 51387-90-7, 2-(2-Aminoethyl)-1-methylpyrrolidine 60923-28-6, 2-(2-Aminoethyl)-1-ethylpyrrolidine 63512-12-9, N-(1-Anthracenyl)acetamide 140937-28-6, 7-Chloro-1,9-Oxalylanthracene 160555-07-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dibenz[de,h]**isoquinoline**-1,3-diones antitumor agents)

INDEX TERM: 36761-80-5P, N-(2-Anthracenyl)acetamide 54440-57-2P, Anthracene-1,9-dicarboxylic anhydride 54440-58-3P 140937-15-1P 140937-16-2P, 7-ChloroAnthracene-1,9-dicarboxylic acid 140937-17-3P 140937-18-4P, 10-ChloroAnthracene-1,9-dicarboxylic acid 140937-19-5P 140937-20-8P 140937-21-9P, 10-MethylAnthracene-1,9-dicarboxylic acid 140937-22-0P, 2-AcetylaminoAnthracene-1,9-dicarboxylic acid 140937-23-1P, 6-AcetylaminoAnthracene-1,9-dicarboxylic acid 140937-24-2P, 7-AcetylaminoAnthracene-1,9-dicarboxylic acid 160555-08-8P, 7-Amino-1,2,3,4-tetrahydroanthracene 160555-09-9P, 4-ChloroAnthracene-1,9-dicarboxylic acid 160555-10-2P, 4-MethylAnthracene-1,9-dicarboxylic acid 160555-11-3P 160555-12-4P 160555-13-5P 160555-15-7P 160555-16-8P, 4-AcetylaminoAnthracene-1,9-dicarboxylic acid 160555-17-9P, 5-AcetylaminoAnthracene-1,9-dicarboxylic acid 160555-18-0P, 10-AcetylaminoAnthracene-1,9-dicarboxylic acid 160555-19-1P, 7-IodoAnthracene-1,9-dicarboxylic acid 160555-20-4P, 4,5-DiChloroAnthracene-1,9-dicarboxylic acid 160555-21-5P 160555-22-6P, 2-MethoxyAnthracene-1,9-dicarboxylic acid 191799-99-2P 191800-00-7P 191800-01-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dibenz[de,h]**isoquinoline**-1,3-diones antitumor agents)

L7 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:681499 CAPLUS
DOCUMENT NUMBER: 126:42327
ENTRY DATE: Entered STN: 20 Nov 1996
TITLE: 2-[2'-(Dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with Substituents at Positions 4, 8, 9, 10, and 11. Synthesis, Antitumor Activity, and Quantitative Structure-Activity Relationships
AUTHOR(S): Sami, Salah M.; Dorr, Robert T.; Alberts, David S.; Solyom, Aniko M.; Remers, William A.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, University of Arizona, Tucson, AZ, 85721, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(25), 4978-4987
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-6 (Pharmacology)
Section cross-reference(s): 27
OTHER SOURCE(S): CASREACT 126:42327

ABSTRACT:
New 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at the 4, 8, 9, 10, and 11 positions were synthesized. Diazonium salts prepared from aminoazonafides were key intermediates for many of the analogs. Six of the new compds. were more potent than azonafide in a panel of tumor cells including human melanoma and ovarian carcinoma and murine L1210 leukemias. Three of these compds., the 10-OCH3, 10-OC2H5, and 10-F analogs, had better ratios of cardiotoxicity to tumor-cell toxicity than did azonafide. Eight compds. were not cross-resistant with MDR L1210 leukemia, and the 10-CN analog was more potent against solid tumor cells than leukemia cells. The 9-OH, 10-CN, and 10-F analogs had high potency against both sensitive and resistant cell lines of MFX 7 breast carcinoma and WiDr colon carcinoma and sensitivity A599 lung carcinoma. Advantages of the 10-Cl, 10-NH2, and 10-CN analogs over azonafide were apparent in P388 leukemia in mice, and the 10-CN analog was more effective than doxorubicin in this assay. Qual. structure-activity relationship studies revealed significant correlations between the DNA binding strength of 8- and 10-substituted azonafides, as measured by ΔTm, and toxicity to tumor cells. There also were correlations between substituent size, as measured by MR, and cytotoxicity for 9- and 10-substituted azonafides and between MR and ΔTm for 4- and 11-substituted azonafides. Lipophilicity of substituents (π) correlated with cytotoxicity for 9-, 10-, and 11-substituted azonafides. These results lend support to a model in which DNA binding strength influences cytotoxic potency, and lipophilicity increases DNA binding whereas large substituents decrease it.

SUPPL. TERM: azonafide deriv prepn antitumor activity QSAR

INDEX TERM: Lung, neoplasm
Ovary, neoplasm
(carcinoma, inhibitors; synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Toxicity
(cardiotoxicity; synthesis, antitumor and cardiotoxic activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Antitumor agents
(colon carcinoma; synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Intestine, neoplasm
(colon, carcinoma, inhibitors; synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Antitumor agents
(leukemia; synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Antitumor agents
(lung carcinoma; synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Antitumor agents
(melanoma; synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Antitumor agents

(ovary carcinoma; synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Antitumor agents
QSAR (structure-activity relationship)
(synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: Heart
(toxicity; synthesis, antitumor and cardiotoxic activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: 84-58-2, 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
21454-60-4, 2-Fluoroanthracene 22362-94-3, 2-Iodoanthracene 140917-74-4 140917-75-5 140937-28-6 160555-08-8 185038-58-8 185038-59-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: 97359-88-1P 140937-16-2P 160555-19-1P 160555-21-5P 160555-22-6P 185038-57-7P 185038-60-2P 185038-61-3P 185038-65-7P 185038-66-8P 185038-69-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: 140937-11-7P 140937-12-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: 140917-86-8 140917-87-9
ROLE: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: 185038-63-5P 185038-64-6P 185038-67-9P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: 140917-67-5DP, Azonafide, derivs. 140917-77-7P 140917-98-2P 140917-99-3P 140918-00-9P 140918-18-9P 140918-19-0P 140918-20-3P 140918-22-5P 140918-23-6P 140918-24-7P 140918-27-0P 140918-28-1P 140918-30-5P 140918-32-7P 160554-78-9P 160554-81-4P 160554-86-9P 160554-90-5P 160554-95-0P 160554-96-1P 160554-99-4P 160555-01-1P 185038-62-4P 185038-68-0P
ROLE: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, antitumor activity, and QSAR of

2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h] **isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

INDEX TERM: 23214-92-8 65271-80-9, Mitoxanthrone **69408-81-7**, Amonafide 140917-67-5, Azonafide
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis, antitumor activity, and QSAR of 2-[2'-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h] **isoquinoline**-1,3-diones with substituents at positions 4, 8, 9, 10, and 11)

L7 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:620024 CAPLUS
DOCUMENT NUMBER: 125:265022
ENTRY DATE: Entered STN: 18 Oct 1996
TITLE: Molecular modeling of DNA-drug complexes as a tool in the design of new antitumor agents
AUTHOR(S): Remers, W. A.; Bear, S.; Hill, G. C.; Rao, S. N.
CORPORATE SOURCE: Department Pharmacology and Toxicology, University Arizona, Tucson, AZ, 85721, USA
SOURCE: Series in Mathematical Biology and Medicine (1995), Volume Date 1994, 5(Computational Medicine, Public Health, and Biotechnology, Pt. 1), 49-64
CODEN: SMBMFO
PUBLISHER: World Scientific
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-3 (Pharmacology)
ABSTRACT:
Simulations based on mol. dynamics successfully predicted sequence selectivity for the covalent complex formed between reduced mitomycin C and DNA segments. A model was derived for the DNA-intercalative binding of amonafide and azonafide, compds. based on 2-[2'-(dimethylamino) ethyl]-1,2-dihydro-3H-benz(de) **isoquinoline**-1,3-diones. It showed that intercalation was possible in a number of different modes, with the side chain in either the major or the minor groove. There was a difference in binding enthalpy favoring azonafide when the simulation was made in vacuum. Solvation simulations indicated nearly equal binding enthalpies, but an advantage for DNA binding of azonafide resulted from a lower desolvation enthalpy relative to that of the more polar amonafide. Other applications of mol. modeling included the modes of action of DNA-alkylating minor groove binders and the absolute chemical of quinocarcin.

SUPPL. TERM: mol modeling DNA antitumor drug complex
INDEX TERM: Molecular modeling
Neoplasm inhibitors
(mol. modeling of DNA-drug complexes as a tool in design of new antitumor agents)
INDEX TERM: Deoxyribonucleic acids
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mol. modeling of DNA-drug complexes as a tool in design of new antitumor agents)
INDEX TERM: Enthalpy and Enthalpy function
(mol. modeling of DNA-drug complexes as a tool in design of new antitumor agents in relation to binding energy)
INDEX TERM: Molecular association
(intercalation, mol. modeling of DNA-drug complexes as a tool in design of new antitumor agents)
INDEX TERM: 50-07-7, Mitomycin C **69408-81-7**, Amonafide
84573-33-1, Quinocarcin 140917-67-5, Azonafide
ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study,

unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mol. modeling of DNA-drug complexes as a tool in design of new antitumor agents)

L7 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:98711 CAPLUS
DOCUMENT NUMBER: 124:249633
ENTRY DATE: Entered STN: 16 Feb 1996
TITLE: Synthesis, structure and antitumor activity of new benz[d,e]**isoquinoline**-1,3-diones
AUTHOR(S): Brana, M. F.; Castellano, J. M.; Moran, M.; Emling, F.; Kluge, M.; Schlick, E.; Klebe, G.; Walker, N.
CORPORATE SOURCE: Knoll S. A., Madrid, Spain
SOURCE: Arzneimittel-Forschung (1995), 45(12), 1311-18
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-3 (Pharmacology)
Section cross-reference(s): 27
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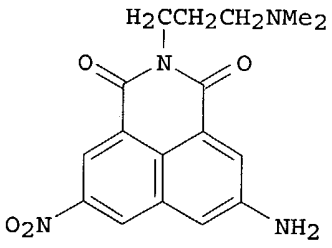

I

ABSTRACT:
New benz[d,e]**isoquinoline**-1,3-diones related to mitonafide and amonafide with double substitution on the chromophore and branched side chains have been synthesized and their biol. activity determined Mol. modeling studies of I based on x-ray crystallog. data of mitonafide have shown that the aromatic system intercalates between GC steps of DNA. The in vitro cytotoxic test data using CX-1 and LX-1 cells showed higher cytotoxic activities in disubstituted derivs. compared to both lead compds. Some of the compds. have been selected for in vivo test using L1210 tumor cells and CX-1 cells. Two of them have shown promising activity as good candidates for clin. development.

SUPPL. TERM: benzisoquinolinedione prepn antitumor agent structure
INDEX TERM: Crystal structure
Molecular modeling
(mol. modeling of interaction of benz[d,e]isoquinolinedione with DNA in relation to crystal structure)
INDEX TERM: Deoxyribonucleic acids
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mol. modeling of interaction of benz[d,e]isoquinolinedione with DNA in relation to crystal structure)
INDEX TERM: Neoplasm inhibitors
(synthesis and structure and antitumor activity of new benz[d,e]isoquinolinediones against human and laboratory animal cells)

INDEX TERM: Molecular structure-biological activity relationship
(neoplasm-inhibiting, synthesis and structure and antitumor activity of new benz[d,e]isoquinolinediones against human and laboratory animal cells)

INDEX TERM: **117611-08-2P 117611-11-7P** 117611-18-4P
174908-32-8P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and structure and antitumor activity of new benz[d,e]isoquinolinediones against human and laboratory animal cells)

INDEX TERM: **117611-10-6P 117611-12-8P**
117611-13-9P 117611-15-1P
135997-04-5P 135997-05-6P
135997-06-7P 135997-07-8P
135997-08-9P 135997-09-0P 174908-28-2P
174908-29-3P **174908-30-6P**
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and structure and antitumor activity of new benz[d,e]isoquinolinediones against human and laboratory animal cells)

INDEX TERM: 54824-17-8, Mitonafide **69408-81-7**, Amonafide
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and structure and antitumor activity of new benz[d,e]isoquinolinediones against human and laboratory animal cells)

INDEX TERM: 108-24-7, Acetic anhydride **174908-31-7**
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and structure and antitumor activity of new benz[d,e]isoquinolinediones against human and laboratory animal cells)

L7 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:413298 CAPLUS
DOCUMENT NUMBER: 123:83170
ENTRY DATE: Entered STN: 15 Mar 1995
TITLE: Amino-Substituted 2-[2-(Dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones. Synthesis, Antitumor Activity, and Quantitative Structure-Activity Relationship
AUTHOR(S): Sami, Salah M.; Dorr, Robert T.; Solyom, Aniko M.; Alberts, David S.; Remers, William A.
CORPORATE SOURCE: Department of Pharmacology/Toxicology and Cancer Center, University of Arizona, Tucson, AZ, 85721, USA
SOURCE: Journal of Medicinal Chemistry (1995), 38(6), 983-93
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
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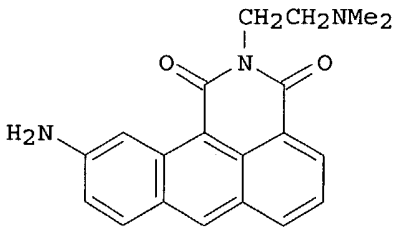

I

ABSTRACT:
Sets of 2-[2-(dimethylamino)ethyl]-1,2-dihydro-3H-dibenz[de,h] ***isoquinoline*** -1,3-diones, e.g., I, with amino and acylamino groups at each of the eight positions on the anthracene nucleus were synthesized from appropriately substituted anthracenes. Their evaluation in in vitro antitumor and cardiotoxicity assays revealed a very strong dependence of potency on the position of substitution. Certain compds., including the 4-, 5-, 7-, and 9-amino derivs., showed significantly higher potency than the unsubstituted parent compound, azonafide. Among them, 7-aminoazonafide had low cardiotoxicity relative to cytotoxicity. In general, the acetylamino analogs were less potent than the amino derivs. against tumor cells and neonatal rat heart myocytes; however, 5-(acetylamino)azonafide was highly cardiotoxic. 9-Aminoazonafide was more efficacious than azonafide or amonafide against P388 leukemia in mice. Statistically significant correlations were made between the ability of amino analogs to increase the transition melt temperature of DNA and their potency against solid tumors, leukemia cells, or cardiac myocytes.

SUPPL. TERM: dibenzisoquinolinedione dimethylaminoethyl amino acylamino deriv cytotoxicity; antitumor activity dimethylaminoethyldibenzisoquinolinedione amino acylamino deriv; cardiotoxicity dimethylaminoethyldibenzisoquinolinedi one amino acylamino deriv; azonafide amino acylamino analog antitumor activity; DNA melt temp aminoazonafide effect; QSAR dimethylaminoethyldibenzisoquinolinedione amino acylamino deriv cytotoxicity

INDEX TERM: Quantitative structure-activity relationship
(antitumor activities and DNA binding properties of azonafide amino analogs)

INDEX TERM: Neoplasm inhibitors
(azonafide amino analogs)

INDEX TERM: Deoxyribonucleic acids
ROLE: PRP (Properties)
(effect of azonafide amino analogs on transition melt temperature of)

INDEX TERM: Toxins
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cardio-, azonafide amino analogs)

INDEX TERM: 165056-09-7 165056-10-0
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor and cardiotoxic activities of)

INDEX TERM: 165055-88-9P 165055-89-0P 165055-90-3P 165055-91-4P
165055-92-5P 165055-93-6P 165055-94-7P 165055-95-8P
165055-96-9P 165055-97-0P 165055-98-1P 165055-99-2P
165056-00-8P 165056-01-9P 165056-02-0P 165056-03-1P
165056-04-2P 165056-05-3P 165056-06-4P
165056-07-5P 165056-08-6P

ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(antitumor and cardiotoxic activities of)

INDEX TERM: **69408-81-7DP**, Amonafide, analogs 140917-67-5DP, analogs
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor and cardiotoxic activities of)

INDEX TERM: 613-13-8, 2-Aminoanthracene 716-53-0, 9-Chloroanthracene 3586-89-8, Anthracene, 1,2,3,4-tetrahydro-6-nitro- 4985-70-0, 1-Chloroanthracene 36761-80-5, 2-Acetamidoanthracene 37170-96-0, 9-Acetamidoanthracene 54440-57-2, 1H,3H-Anthra[1,9-cd]pyran-1,3-dione 63512-12-9, 1-Acetamidoanthracene 140917-78-8 160554-94-9 160555-07-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor and cardiotoxic activities of azonafide amino analogs)

INDEX TERM: 140917-74-4P 140917-75-5P 140917-83-5P 140917-84-6P 140917-85-7P **140918-03-2P** 140918-06-5P 140918-10-1P 140918-14-5P 140918-17-8P 140937-12-8P 140937-13-9P 140937-14-0P 140937-25-3P 140937-26-4P 140937-27-5P 160554-76-7P 160555-08-8P, 2-Anthracenamine, 5,6,7,8-tetrahydro- 160555-12-4P 160555-13-5P 165055-85-6P 165055-87-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor and cardiotoxic activities of azonafide amino analogs)

INDEX TERM: 140917-86-8P 140917-87-9P 140917-88-0P 140918-02-1P 140918-07-6P 140918-15-6P 140918-31-6P 140937-11-7P 160554-75-6P 160555-11-3P 165055-86-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antitumor and cardiotoxic activities of azonafide amino analogs)

L7 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:319736 CAPLUS
DOCUMENT NUMBER: 122:105693
ENTRY DATE: Entered STN: 01 Feb 1995
TITLE: Preparation of N-aminoalkyl-1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones as anticancer agents
INVENTOR(S): Alberts, David S.; Dorr, Robert T.; Remers, William A.; Sami, Salah M.
PATENT ASSIGNEE(S): Research Corp. Technologies, Inc., USA
SOURCE: PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D221-18
SECONDARY: C07D401-04; C07D401-06; A61K031-435
CLASSIFICATION: 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

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WO 9406771	A1	19940331	WO 1993-US8640	19930913
W: AU, CA, JP, US				

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9351278 A1 19940412 AU 1993-51278 19930913
EP 660824 A1 19950705 EP 1993-922191 19930913
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, SE
JP 08501312 T2 19960213 JP 1993-508237 19930913
JP 3543196 B2 20040714 JP 1994-508237 19930913
US 5635506 A 19970603 US 1993-142283 19931118
PRIORITY APPLN. INFO.: US 1992-943634 A2 19920911
US 1990-543596 B1 19900626
US 1991-803314 B2 19911204
WO 1993-US8640 W 19930913

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9406771	ICM	C07D221-18
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OTHER SOURCE(S): MARPAT 122:105693

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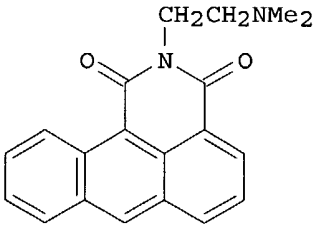

II

ABSTRACT:
RADNR12R13 [I; A = bond, (CR4R5)1-5, cycloalkylene, arylene; D = bond; DNR12 = heterocyclyl; R = (un)substituted 1,2-dihydro-3H-1,3-dioxodibenz[de,h]isoquinolin-2-yl; R4,R5 = H, alkyl; R12,R13 = H, alkyl; NR12R13 = heterocyclyl] were prepared Thus, anthracene-1,9-dicarboxylic acid anhydride (preparation given) was cyclocondensed with N,N-dimethylethylenediamine to give title compound II. Extensive data for anticancer activity of I are given.

SUPPL. TERM: dibenzisoquinolinediones aminoalkyl anticancer agent
INDEX TERM: Neoplasm inhibitors
(N-(aminoalkyl)dibenzisoquinolinediones)
INDEX TERM: 6929-82-4P 22023-39-8P
ROLE: SPN (Synthetic preparation); FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in preparation of anticancer agent)
INDEX TERM: 36761-80-5P, Acetamide, N-(2-anthracenyl) 54440-57-2P, Anthracene-1,9-dicarboxylic anhydride 54440-58-3P
140937-15-1P 140937-16-2P 140937-17-3P 140937-18-4P
140937-19-5P 140937-20-8P 140937-21-9P 140937-22-0P
140937-23-1P 140937-24-2P 140937-25-3P 140937-26-4P
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160555-19-1P 160555-20-4P 160555-21-5P 160555-22-6P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of anticancer agent)
INDEX TERM: 140917-67-5P 140917-68-6P 140917-69-7P 140917-70-0P
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160555-04-4P 160555-05-5P 160555-23-7P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as anticancer agent)

INDEX TERM: 99-98-9, N,N-Dimethyl-p-phenylenediamine 108-00-9, N,N-Dimethylethylenediamine 109-55-7, 3-Dimethylaminopropylamine 109-81-9, N-Methylethylenediamine 111-41-1, 2-(2-Aminoethylamino)ethanol 140-31-8, N-(2-Aminoethyl)piperazine 462-08-8, 3-Aminopyridine 529-85-1, 9-Fluoroanthracene 610-48-0, 1-Methylanthracene 613-12-7, 2-Methylanthracene 613-13-8, 2-Aminoanthracene 716-53-0, 9-Chloroanthracene 779-02-2, 9-Methylanthracene 1564-64-3, 9-Bromoanthracene 2038-03-1, 4-(2-Aminoethyl)morpholine 2706-56-1, 2-(2-Aminoethyl)pyridine 3586-89-8 3731-52-0, 3-Aminomethylpyridine 4025-37-0, 1-(2-Aminoethyl)aziridine 4985-70-0, 1-Chloroanthracene 4985-85-7, N-(3-Aminopropyl)diethanolamine 6789-94-2, 3-Amino-1-ethylpiperidine 7154-73-6, 1-(2-Aminoethyl)pyrrolidine 14381-66-9, 1,8-DiChloroanthracene 22362-90-9, 1-Iodoanthracene 22362-94-3, 2-Iodoanthracene 26116-12-1, 2-Aminomethyl-1-ethylpyrrolidine 27578-60-5, 1-(2-Aminoethyl)piperidine 37170-96-0, 9-(Acetylamino)anthracene 42298-28-2, 2-Methoxyanthracene 51384-67-9, Anthracene-1,9-dicarboxylic acid 51387-90-7, 2-(2-Aminoethyl)-1-methylpyrrolidine 63512-12-9, Acetamide, N-(1-anthracenyl) 160555-06-6 160555-07-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of anticancer agent)

L7 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:168954 CAPLUS
DOCUMENT NUMBER: 118:168954
ENTRY DATE: Entered STN: 01 May 1993
TITLE: 2-Substituted 1,2-dihydro-3H-dibenz[de,h]**isoquinoline**-1,3-diones. A new class of antitumor agent
AUTHOR(S): Sami, Salah M.; Dorr, Robert T.; Alberts, David S.; Remers, William A.
CORPORATE SOURCE: Dep. Pharm. Sci., Univ. Arizona, Tucson, AZ, 85721,

USA
SOURCE: Journal of Medicinal Chemistry (1993), 36(6), 765-70
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

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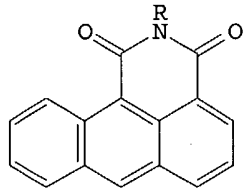
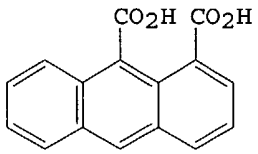
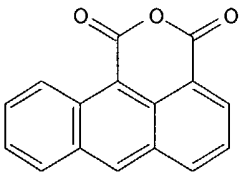


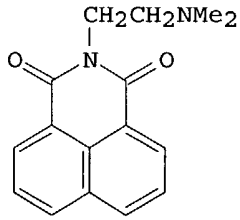
I



II



III



IV

ABSTRACT:
Title compds. I [R = CH2CH2NMe2, CH2CH2NHMe, (CH2)3NMe2, CH2CH2NHCH2CH2OH, (CH2)3N(CH2CH2OH)2, 2-(1-pyrrolidinyl), 2-piperidinoethyl, 2-(1-methyl-1-pyrrolidinyl)ethyl, 2-morpholinoethyl, 2-(2-pyridyl)ethyl, imidazol-2-yl, etc.] were prepared by treating diacid II or anhydride III with the appropriate amines. I are a new class of antitumor agents, having structural analogy to amonafide (IV), but differing by the addition of a fourth ring in the nucleus. Thirteen of the 19 new compds. had greater growth inhibitory potency than amonafide in a panel of cultured murine and human tumor cells using the sulforhodamine B and MTT dye assays. The most active agents were similarly more toxic than amonafide to normal neonatal rat myocytes in vitro, but they had better chemotherapeutic indexes. I (R = CH2CH2NMe2) (azonafide) showed high potency against a panel of cultured human colon cancer cells and it was active against i.p. P388 leukemia and s.c. B16 melanoma in mice. Preliminary structure-activity correlations suggest that the basicity of the side-chain nitrogen and the length of side chain are important determinants of antitumor potency in vitro. Steric hindrance and rigidity of the side chains might be other determinants.

SUPPL. TERM: antitumor dihydrodibenzisoquinolinedione; hydrodibenzisoquinolinedione prepn antitumor; dibenzisoquinolinedione dihydro prepn antitumor
INDEX TERM: Neoplasm inhibitors
(dihydrodibenzisoquinolinediones)
INDEX TERM: Molecular structure-biological activity relationship
(neoplasm-inhibiting, of dihydrodibenzisoquinolinediones)
INDEX TERM: **69408-81-7**, Amonafide
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor activity of)
INDEX TERM: 51384-67-9, 1,9-Anthracenedicarboxylic acid
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with amines)
INDEX TERM: 140917-67-5P 140917-68-6P 140917-69-7P 140917-70-0P

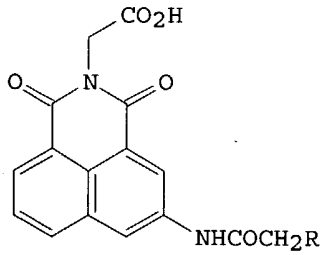
140917-71-1P 140917-72-2P 140917-73-3P 140917-82-4P
140917-90-4P 140917-91-5P 140917-92-6P 140917-93-7P
140917-95-9P 140917-96-0P 146516-60-1P 146516-61-2P
146516-63-4P 146516-64-5P 146516-65-6P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of)

INDEX TERM: 54440-57-2, 1H,3H-Anthra[1,9-cd]pyran-1,3-dione
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with amines)

INDEX TERM: 99-98-9 140-31-8, 1-Piperazineethanamine 462-08-8, 3-Pyridinamine 7720-39-0, 1H-Imidazol-2-amine
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with anthracenedicarboxylic acid anhydride)

INDEX TERM: 108-00-9 109-55-7 109-81-9 111-41-1 1721-30-8, 1-Aziridinamine 2038-03-1, 4-Morpholineethanamine 2706-56-1, 2-Pyridineethanamine 3731-51-9, 2-Pyridinemethanamine 3731-52-0, 3-Pyridinemethanamine 4985-85-7 6789-94-2 7154-73-6, 1-Pyrrolidineethanamine 26116-12-1 27578-60-5, 1-Piperidineethanamine 51387-90-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with anthracenedicarboxylic acid or its anhydride)

L7 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:146632 CAPLUS
DOCUMENT NUMBER: 116:146632
ENTRY DATE: Entered STN: 17 Apr 1992
TITLE: Selective irreversible inhibitors of aldose reductase
AUTHOR(S): Smar, Michael W.; Ares, Jeffrey J.; Nakayama, Toshihiro; Itabe, Hiroyuki; Kador, Peter F.; Miller, Duane D.
CORPORATE SOURCE: Coll. Pharm., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(6), 1117-20
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 7-3 (Enzymes)
GRAPHIC IMAGE:



II, R=Br
III, R=I

ABSTRACT:
A series of 5-substituted 1,3-dioxo-1H-benz[de]**isoquinoline**-2(3H)-acetic acid (alrestatin) analogs were examined as irreversible inhibitors of aldose reductase (I). The 5-α-bromoacetamide and 5-α-iodoacetamide analogs II and III gave irreversible inhibition of aldose reductase, whereas the 5-α-chloroacetamide analog did not show this type of inhibition. Protection studies indicated that irreversible inhibitions occurred at the inhibitor binding site. Comparative irreversible inhibition studies with rat lens I and rat kidney aldehyde reductase indicated that

5-α-haloacetamide analogs II and III are much more effective inhibitors of rat lens I.

SUPPL. TERM: haloacetamido dioxobenzisoquinolineacetate prepn enzyme inhibition; aldose reductase inhibition alrestatin analog; aldehyde reductase inhibition alrestatin analog

INDEX TERM: Kidney, composition
(aldehyde reductase of, of rat, inhibition of, by alrestatin analog)

INDEX TERM: Eye, composition
(lens, aldose reductase of, of rat, inhibition of, by alrestatin analogs)

INDEX TERM: 139584-36-4
ROLE: BIOL (Biological study)
(aldehyde and aldose reductase inhibition by)

INDEX TERM: 103904-10-5
ROLE: BIOL (Biological study)
(aldose reductase inhibition by)

INDEX TERM: **103884-83-9**
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of)

INDEX TERM: 9028-31-3, Aldose reductase
ROLE: PROC (Process)
(inhibition of, of rat eye lens, by alrestatin analogs)

INDEX TERM: 9028-12-0, Aldehyde reductase
ROLE: PROC (Process)
(inhibition of, of rat kidney, by alrestatin analog)

INDEX TERM: 51411-04-2DP, Alrestatin, analogs 139584-33-1P
139584-34-2P 139584-35-3P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and aldose and aldehyde reductases inhibition by)

INDEX TERM: **53497-35-1P**
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with haloacetic anhydride)

L7 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:83557 CAPLUS
DOCUMENT NUMBER: 116:83557
ENTRY DATE: Entered STN: 06 Mar 1992
TITLE: Preparation of 2-(heterocyclyl)-2,3-dihydro-1H-benz[de]**isoquinoline**-1,3-diones as 5-HT3 receptor antagonists
INVENTOR(S): Berger, Jacob; Clark, Robin D.; Eglen, Richard M.; Smith, William L.; Weinhardt, Klaus K.
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D451-04
SECONDARY: C07D451-14; C07D453-02; C07D453-06; C07D487-08; C07D209-80; A61K031-40; A61K031-435
INDEX: C07D487-08, C07D209-00
CLASSIFICATION: 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 457243	A1	19911121	EP 1991-107721	19910513
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				

AU 9176189	A1	19911114	AU 1991-76189	19910429
NO 9101845	A	19911115	NO 1991-1845	19910513
FI 9102317	A	19911115	FI 1991-2317	19910513
CA 2042443	AA	19911115	CA 1991-2042443	19910513
HU 58095	A2	19920128	HU 1991-1587	19910513
JP 04226974	A2	19920817	JP 1991-138246	19910513
ZA 9103605	A	19930127	ZA 1991-3605	19910513
CN 1059724	A	19920325	CN 1991-103292	19910514

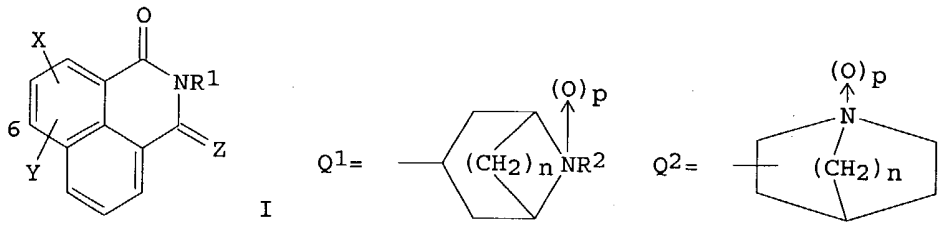
PRIORITY APPLN. INFO.: US 1990-523090 19900514

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 457243	ICM	C07D451-04
	ICS	C07D451-14; C07D453-02; C07D453-06; C07D487-08; C07D209-80; A61K031-40; A61K031-435
	ICI	C07D487-08, C07D209-00

OTHER SOURCE(S): MARPAT 116:83557

GRAPHIC IMAGE:



ABSTRACT:
Title compds. I [Z = O or H,H; X, Y = H, halo, OH, C1-6 alkoxy, PhCH2O, C1-6 alkyl, NO2, (substituted) amino, carbamoyl, C3-6 cycloalkyl; R1 = Q1, Q2, etc.; p = 0, 1; n = 1-3; R2 = H, (substituted) C1-6 alkyl, C3-8 cycloalkyl, (CH2)tR3; R3 = (substituted) thienyl, -pyrrolyl, -furyl, or -Ph; t = 1, 2] were prepared as 5-HT3 receptor antagonists useful as antiemetics and anxiolytics, for example. Thus, a solution of S-3-aminoquinuclidine in xylenes was added dropwise to a boiling solution of 4-nitro-1,8-naphthalic anhydride. The mixture was refluxed 6 h with removal of H2O. Ac2O was added and the solution was heated an addnl. 16 h to give S-I (Z = O, X = 6-NO2, Y = H, R1 = 1-azabicyclo[2.2.2]oct-3-yl). This was hydrogenated over 10% Pd/C to give S-I (X = 6-NH2, all others as above) (II). II·HCl at 1.0 mg/kg i.v. in emetic ferrets reduced the number of retching and vomiting episodes and the time to onset of emesis. Formulations of I were prepared

SUPPL. TERM: azabicyclooctyldihydrobenzisoquinolinedione prepn
serotoninergic antagonist; antiemetic
azabicyclooctyldihydrobenzisoquinolinedione; CNS agent
azabicyclooctyldihydrobenzisoquinolinedione; anxiolytic
azabicyclooctyldihydrobenzisoquinolinedione

INDEX TERM: Analgesics
Antiemetics
Anxiolytics
Cardiovascular agents
Nervous system agents
((heterocyclyl)benzisoquinolinediones)

INDEX TERM: Digestive tract
(disease, treatment of, (heterocyclyl)benzisoquinolinediones for)

INDEX TERM: Headache
(migraine, treatment of, (heterocyclyl)benzisoquinolinediones for)

INDEX TERM: Tranquilizers and Neuroleptics

(minor, (heterocyclyl)benzisoquinolinediones)

INDEX TERM: Neurotransmitter antagonists
(serotoninergic S3, (heterocyclyl)benzisoquinolinediones)

INDEX TERM: 138682-35-6P 138682-36-7P 138682-37-8P 138682-38-9P
138682-39-0P 138682-40-3P 138682-41-4P 138682-42-5P
138682-43-6P 138682-44-7P **138682-45-8P**
138682-46-9P 138682-47-0P 138682-48-1P 138682-49-2P
138682-50-5P 138682-51-6P 138682-52-7P 138682-53-8P
138682-54-9P **138682-55-0P** 138682-56-1P
138682-57-2P 138682-58-3P 138682-59-4P 138682-60-7P
138682-61-8P 138682-63-0P 138682-64-1P 138682-65-2P
138682-66-3P 138682-67-4P 138682-68-5P 138682-69-6P
138682-70-9P 138682-71-0P 138682-72-1P 138682-73-2P
138682-74-3P 138682-75-4P 138682-76-5P 138682-77-6P
138682-78-7P 138682-79-8P 138682-80-1P 138682-81-2P
138704-06-0P 138704-07-1P 138729-48-3P 138752-28-0P
138752-29-1P 138752-30-4P 138752-31-5P 138752-32-6P
138752-33-7P 138752-34-8P 138752-35-9P 138752-36-0P
138752-37-1P 138752-38-2P 138752-39-3P 138752-40-6P
138752-41-7P 138752-42-8P 138752-43-9P 138782-58-8P
149634-96-8P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT3 receptor antagonist)

INDEX TERM: 138682-82-3P 138682-83-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for 5-HT3 receptor antagonists)

INDEX TERM: 81-84-5, 1H,3H-Naphtho[1,8-cd]pyran-1,3-dione 81-86-7, 4-Bromo-1,8-naphthalic anhydride 108-24-7, Acetic anhydride 4053-08-1, 4-Chloro-1,8-naphthalic anhydride 6238-14-8, RS-3-Aminoquinuclidine 6642-29-1, 4-Nitro-1,8-naphthalic anhydride 120570-05-0 123536-15-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of 5-HT3 receptor antagonists)

L7 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:591125 CAPLUS
DOCUMENT NUMBER: 113:191125
ENTRY DATE: Entered STN: 23 Nov 1990
TITLE: The UV-visible absorption and fluorescence of some substituted 1,8-naphthalimides and naphthalic anhydrides
AUTHOR(S): Alexiou, Michael S.; Tychopoulos, Vasiliki; Ghorbanian, Shohreh; Tyman, John H. P.; Brown, Robert G.; Brittain, Patrick I.
CORPORATE SOURCE: Dep. Chem., Brunel Univ., Uxbridge/Middlesex, UB8 3PH, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1972-1999) (1990), (5), 837-42
CODEN: JCPKBH; ISSN: 0300-9580
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 22

ABSTRACT:
Substituted 1,8-naphthalimides and naphthalic anhydrides were prepared and their absorption and fluorescence properties in absolute EtOH were determined In the absence of an alkylamino substituent in the naphthalene ring, the compds. are colorless and weakly fluorescent. In the presence of such a substituent they become yellow and frequently fluoresce strongly with quantum yields on the order of 0.8.

SUPPL. TERM: naphthalimide UV visible fluorescence spectra; naphthalic anhydride UV visible fluorescence spectra

INDEX TERM: Fluorescence
Ultraviolet and visible spectra
(of substituted naphthalimides and naphthalic anhydride)

INDEX TERM: 81-83-4P, 1H-Benz[de]**isoquinoline**-1,3(2H)-dione
3353-99-9P 6914-62-1P 19125-99-6P 35652-30-3P
38842-43-2P 54229-22-0P 54229-23-1P 75852-92-5P
75853-01-9P 75865-44-0P 79238-85-0P 79238-87-2P
79238-88-3P 92874-17-4P 121638-52-6P 121638-53-7P
130001-45-5P 130001-46-6P 130001-47-7P 130001-48-8P
130001-50-2P 130001-51-3P 130001-53-5P 130001-54-6P
130001-55-7P 130010-48-9P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and UV-visible spectrum and fluorescence properties of)

INDEX TERM: 55490-98-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and acetylation and UV-visible spectrum and fluorescence properties of)

INDEX TERM: 84216-52-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and substitution reaction of, with butylamine)

INDEX TERM: 130001-52-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation, UV-visible spectrum and fluorescence properties, and acetylation of)

INDEX TERM: **130001-49-9P**
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation, UV-visible spectrum and fluorescence properties, and reductive alkylation of)

INDEX TERM: 67834-68-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reduction or substitution reaction of, with dimethylamine)

INDEX TERM: 4053-08-1, 4-Chloro-1,8-naphthalic anhydride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with amines, alkylamino imides from)

INDEX TERM: 81-86-7, 4-Bromo-1,8-naphthalic anhydride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with amines, imides from)

INDEX TERM: 81-84-5, 1H,3H-Naphtho[1,8-cd]pyran-1,3-dione
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with ammonia or butylamine, imides from)

INDEX TERM: 3807-78-1 21563-29-1, 2-Bromo-1,8-naphthalic anhydride
34087-02-0, 2-Nitro-1,8-naphthalic anhydride 39061-35-3,
4-Nitro-1,8-phthalimide 42340-35-2 50817-72-6,
2-Chloro-1,8-naphthalic anhydride 52559-36-1,
4-Bromo-1,8-naphthalimide
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with butylamine)

INDEX TERM: 3027-38-1, 3-Nitro-1,8-naphthalic anhydride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with butylamine, imide from)

INDEX TERM: 6642-29-1, 4-Nitro-1,8-naphthalic anhydride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction with amines or hydrazine or reduction of)

L7 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:31965 CAPLUS
DOCUMENT NUMBER: 112:31965

ENTRY DATE: Entered STN: 04 Feb 1990
TITLE: Genotoxicity of [1H]benz[de]**isoquinoline** -1,3[2H]dione, 5 amino-2-, [2-(dimethylamino) ethyl] (BIDA) in human lymphocytes
AUTHOR(S): Savaraj, Niramol; Liang, Jan; Lu, Katherine; Feun, Lynn G.; Hsu, T. C.
CORPORATE SOURCE: V.A. Med. Cent., Miami, FL, 33125, USA
SOURCE: Cancer Investigation (1989), 7(2), 117-21
CODEN: CINVD7; ISSN: 0735-7907
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 4-6 (Toxicology)
ABSTRACT:

Genotoxicity was studied of BIDA in cultured human lymphocytes stimulated with PHA for 72 h. Doses of 0.1, 0.25, 0.5, 0.75, and 1 μg BIDA/mL were added to the culture at 1 h (G2 phase), and 6 h (S/G2 phase) before harvesting. Cells were harvested at the end of the 72-h culture period with 1-h colcemid treatment to accumulate mitosis, and further prepared by standard cytogenetic technique. BIDA induced chromatic type breakages and chromatid exchanges at both 1 h and 6 h. The mean number of breakages per cell was 0, 0.1, 1.0, and 1.7 after treatment with 0.1, 0.25, and 0.75 μg/mL, resp. At 1 μg/mL, BIDA severely inhibited cell progression and very few mitoses were observed At 6 h the mean number of breakages per cell was 0.3 at 0.25 μg/mL and 1.2 at 0.5 μg/mL. Very few cells entered mitosis at 0.75 and 1 μg/mL. To study the effect of BIDA on cells in G0 and G1, BIDA (0.75 μg/mL) was added for 1 h to the cultures at the beginning of culture (G0), or 24 h after (G1) culture initiation. Afterward, cells were washed and reincubated in the conditioned medium for 71 or 47 h. No chromosomal aberrations were seen in these expts. The number of chromatid breaks was minimal (0.1 to 0.4/cell). The study suggests that BIDA induces chromatid type aberrations during G2 and S phases. The absence of chromosome type aberrations in cells treated during G0 and G1 suggests that either BIDA has no effect on these cells or that damaged cells fail to progress through S and G2 to reach mitosis.

SUPPL. TERM: aminodimethylaminoethylbenzoisoquinolinedione genotoxicity lymphocyte
INDEX TERM: Lymphocyte
(aminodimethylaminoethanol benzoisoquinolinedione genotoxicity in human, cell cycle in relation to)
INDEX TERM: Chromatid
(aminodimethylaminoethylbenzoisoquinolinedione effect on, of human lymphocytes, cell cycle in relation to)
INDEX TERM: Cell cycle
(aminodimethylaminoethylbenzoisoquinolinedione genotoxicity in human lymphocytes in relation to)
INDEX TERM: Chromosome
(aminodimethylaminoethylbenzoisoquinolinedione induction of breakage of, in human lymphocytes, cell cycle in relation to)
INDEX TERM: Cell division
(mitosis, aminodimethylaminoethylbenzoisoquinolinedione inhibition of, in human lymphocytes)
INDEX TERM: **69408-81-7**
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(genotoxicity of, in human lymphocytes, cell cycle in relation to)

L7 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:504355 CAPLUS
DOCUMENT NUMBER: 109:104355
ENTRY DATE: Entered STN: 01 Oct 1988
TITLE: In vitro activity of amonafide against primary human tumors compared with the activity of standard agents

AUTHOR(S): Ajani, Jaffer A.; Baker, Fraser L.; Spitzer, Gary
CORPORATE SOURCE: M. D. Anderson Hosp., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Investigational New Drugs (1988), 6(2), 79-85
CODEN: INNDDK; ISSN: 0167-6997
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-6 (Pharmacology)
ABSTRACT:
Amonafide, one of a series of benz[de]-**isoquinoline**-1,3-dione compds., is now entering phase-II clin. trials. Amonafide, exposed continuously for 5 days at 4 different concns. against 56 primary human tumors, was tested in vitro. The drug concentration range used was based on amonafide's inhibitory activity against human bone marrow cells. The antitumor activity of 5-fluorouracil, mitomycin C, cisplatin, and etoposide against tumors from this panel of 56 was compared with that of amonafide at in vitro concns. equitoxic against human bone marrow cells. Amonafide was active against only 12% of tumors compared with standard agents, which were active against more than 40% of tumors in the human bone marrow inhibitory range. Apparently, amonafide is less likely to be clin. active against human solid tumors than the standard agents.

SUPPL. TERM: amonafide antitumor
INDEX TERM: Neoplasm inhibitors
(amonafide as, of humans)
INDEX TERM: **69408-81-7**, Amonafide
ROLE: BIOL (Biological study)
(solid tumors of humans inhibition by)

L7 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:94420 CAPLUS
DOCUMENT NUMBER: 108:94420
ENTRY DATE: Entered STN: 19 Mar 1988
TITLE: New benz[de]**isoquinoline**-1,3-diones, their preparation, and their use as tumor inhibitors
INVENTOR(S): Fernandez Brana, Miguel; Castellano Berlanga, Jose Maria; Schlick, Erich; Keilhauer, Gerhard
PATENT ASSIGNEE(S): Knoll A.-G. Chemische Fabriken, Fed. Rep. Ger.
SOURCE: Ger. Offen., 3 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: C07D221-14
SECONDARY: A61K031-47; A61K045-05
CLASSIFICATION: 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

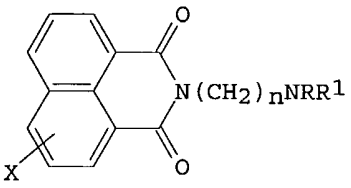
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3614414	A1	19871105	DE 1986-3614414	19860429
EP 243841	A1	19871104	EP 1987-105793	19870418
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
JP 63022078	A2	19880129	JP 1987-102168	19870427
DK 8702151	A	19871030	DK 1987-2151	19870428
FI 8701850	A	19871030	FI 1987-1850	19870428
NO 8701766	A	19871030	NO 1987-1766	19870428
AU 8772125	A1	19871105	AU 1987-72125	19870428
HU 44517	A2	19880328	HU 1987-1900	19870428
ZA 8703007	A	19890125	ZA 1987-3007	19870428
PRIORITY APPLN. INFO.:			DE 1986-3614414	19860429

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

DE 3614414	ICM	C07D221-14
	ICS	A61K031-47; A61K045-05

GRAPHIC IMAGE:



I

ABSTRACT:
Benzisoquinolinediones I [X = HO, NO2, alkoxy, (di)(alkyl)amino, alkylcarbonylamino, alkoxycarbonylamine, alkyl, CF3, H, halo; n = 0-4; R = H, hydroxyalkyl; R1 = hydroxyalkyl, X ≠ 5-NO2 or H and n ≠ 2 when R = H and R1 = hydroxyethyl] and their salts with physiol. tolerable acids, useful as antitumor and antileukemia agents (no data), are prepared A mixture of 3-nitro-1,8-naphthalic acid and H2N(CH2)3N(CH2CH2OH)2 in EtOH was stirred for 5 h at room temperature to give 83% I (X = 5-NO2, n = 3, R = R1 = CH2CH2OH).

SUPPL. TERM:	benzisoquinolinedione tumor leukemia inhibitor prepn
INDEX TERM:	Neoplasm inhibitors (benzisoquinolinedione derivs.)
INDEX TERM:	Neoplasm inhibitors (leukemia, benzisoquinolinedione derivs.)
INDEX TERM:	37140-22-0, 3-Nitro-1,8-naphthalic acid ROLE: RCT (Reactant); RACT (Reactant or reagent) (cyclization of, with (aminopropyl)diethanolamine)
INDEX TERM:	81-84-5D, Naphthalic anhydride, derivs. ROLE: RCT (Reactant); RACT (Reactant or reagent) (cyclization of, with aminoalkylamines)
INDEX TERM:	4985-85-7 ROLE: RCT (Reactant); RACT (Reactant or reagent) (cyclization of, with nitronaphthalic acid)
INDEX TERM:	58232-31-8P 109858-35-7P 112937-49-2P 112937-50-5P **112937-51-6P** 112937-52-7P 112937-53-8P 112937-54-9P 112937-55-0P 112937-56-1P 112937-57-2P 112937-58-3P **112937-59-4P** 112937-60-7P 112937-61-8P **112937-62-9P** 112937-63-0P 112937-64-1P 112937-65-2P 112937-66-3P 112937-67-4P 112937-68-5P 112937-69-6P 112937-70-9P ROLE: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as tumor and leukemia inhibitor)

L7 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1986:516990 CAPLUS
DOCUMENT NUMBER:	105:116990
ENTRY DATE:	Entered STN: 03 Oct 1986
TITLE:	Industrial production of 5-amino-2[2-(dimethylamino)ethyl]benzo[d,e]**isoquinoline**-1,3-dione
INVENTOR(S):	Fernandez Brana, Miguel; Alvarez Ossorio, Antonio Martinez Sanz Rafael Perez; Martinez Sanz, Antonio; De Gamboa, Christina Roldan Fernandez; Garrido Garcia, Jesus
PATENT ASSIGNEE(S):	Laboratorios Made S. A. , Spain
SOURCE:	Span., 6 pp.

CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
INT. PATENT CLASSIF.:
MAIN: C07D217-24
SECONDARY: C07C087-08
CLASSIFICATION: 45-4 (Industrial Organic Chemicals, Leather, Fats, and Waxes)
Section cross-reference(s): 27
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 535838	A1	19850901	ES 1984-535838	19840912
US 5183821	A	19930202	US 1991-728025	19910708
PRIORITY APPLN. INFO.:			US 1983-533542	19830919
			US 1986-864009	19860516
			US 1989-296340	19890109

PATENT CLASSIFICATION CODES:

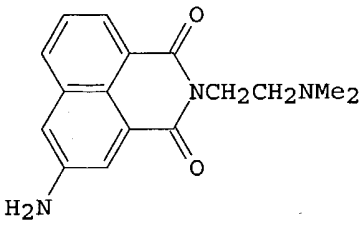
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
ES 535838	ICM	C07D217-24
	ICS	C07C087-08

ABSTRACT:
The reduction of 2-[2-(dimethylamino)ethyl]-5-nitroenzo[d,e]**isoquinoline**-1,3-dione (I) with hydrazine in the presence of a Pd catalyst in a solvent, e.g., EtOH, gives 5-amino-2-[2-(dimethylamino)ethyl]benzo[d,e]***isoquinoline*** -1,3-dione (II) of high purity in nearly quant. yield. Thus, 3.0 kg I was dissolved in 75 l EtOH along with 75 g Pd (10% Pd/C) with heating to reflux and stirring, and 3.0 l 80% hydrazine hydrate was added during 1 h with addnl. heating and stirring for 3 h to prepare II.

SUPPL. TERM: aminodimethylaminoethylbenzoisoquinolinedione manuf; benzoisoquinonedione aminodimethylaminoethyl manuf; isoquinonedione aminodimethylaminoethylbenzo manuf; nitrodimethylaminoethylbenzoisoquinolinedione redn hydrazine
INDEX TERM: **69408-81-7P**
ROLE: PREP (Preparation)
(manufacture of, by reduction of nitro compound with hydrazine)
INDEX TERM: 302-01-2, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reduction by, of (dimethylaminoethyl)nitrobenzoisoquinolinedione)
INDEX TERM: 54824-17-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reduction of, to amine, by hydrazine)

L7 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:89672 CAPLUS
DOCUMENT NUMBER: 102:89672
ENTRY DATE: Entered STN: 22 Mar 1985
TITLE: Computer assisted structure-activity correlations. Evaluation of benzo(de)**isoquinoline**-1,3-diones and related compounds as antitumor agents
AUTHOR(S): Paull, K. D.; Nasr, M.; Narayanan, V. L.
CORPORATE SOURCE: Div. Cancer Treat., Natl. Cancer Inst., Bethesda, MD, 20205, USA
SOURCE: Arzneimittel-Forschung (1984), 34(10), 1243-6
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-3 (Pharmacology)

GRAPHIC IMAGE:



I

ABSTRACT:
Computer assisted evaluations of benzo(de)**isoquinoline**-1,3-diones and related compds. screened for antitumor activity against P388 lymphocytic leukemia and L1210 lymphoid leukemia are presented. Two important features necessary for good anticancer activity are the nature of the imide side-chain and the type of substituent on the aromatic portion. Based on these considerations NSC 308847 [1H-benzo(de)**isoquinoline**-1,3(2H)dione,5-amino-2-(2-dimethylaminoethyl)](I) **[69408-81-7]** has been selected for preclin. toxicol. studies.

SUPPL. TERM: antitumor benzoisoquinolinedione structure

INDEX TERM: Neoplasm inhibitors
(benzo(de)isoquinolinediones)

INDEX TERM: Computer application
(in benzo(de)isoquinolinedione structure-antitumor activity evaluation)

INDEX TERM: Molecular structure-biological activity relationship
(neoplasm-inhibiting, of benzo(de)isoquinolinediones)

INDEX TERM: 6914-62-1 54824-17-8 54824-20-3 66266-36-2
69408-81-7 94887-57-7 94887-58-8
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of, computer assisted structure-activity correlations in)

INDEX TERM: 81-33-4 81-83-4D, derivs. 5690-24-4 22177-46-4
67139-78-0 70655-01-5 73771-32-1 94210-30-7
94887-59-9 94887-60-2 94887-61-3 94887-62-4
94887-63-5 94887-64-6 94887-65-7 94887-66-8
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of, structure in relation to, computer assisted evaln. of)

L7 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

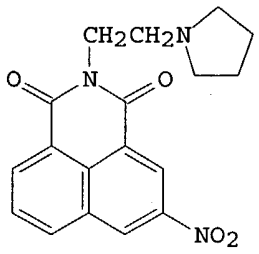
ACCESSION NUMBER: 1985:17173 CAPLUS
DOCUMENT NUMBER: 102:17173
ENTRY DATE: Entered STN: 26 Jan 1985

TITLE: In vivo effects of three derivatives of benzo[de]**isoquinoline**-1,3-dione on Trypanosoma cruzi

AUTHOR(S): Castanys-Cuello, S.; Osuna-Carrillo, A.; Gamarro-Conde, F.; Ruiz-Perez, L. M.; Jeronimo-Gonzalez, N.; Jeronimo-Gonzalez, M. C.; Fernandez-Brana, M.; Martinez-Roldan, C.
CORPORATE SOURCE: Dep. Parasitol., Fac. Farm., Granada, Spain

SOURCE: Laboratorio (Granada, Spain) (1984), 459, 177-87
CODEN: LABRA9; ISSN: 0023-6691

DOCUMENT TYPE: Journal
LANGUAGE: Spanish
CLASSIFICATION: 1-5 (Pharmacology)
GRAPHIC IMAGE:



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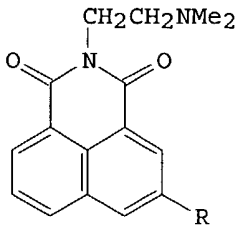
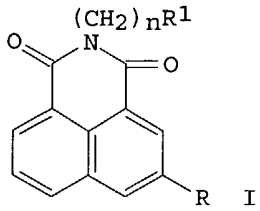


II, R=NO_2
III, R=NH_2

ABSTRACT:
The effects of M-12210 (I) [54824-20-3] M-4212 (II) [54824-17-8], and FA-142 (III) [**69408-81-7**] on mice previously infected with T. cruzi were studied. I and III increased the survival of the mice. The protective effect of I was decreased when the compound had previously been intercolated with DNA, but its toxic effect was also diminished.

SUPPL. TERM: benzoisoquinolinedione Trypanosoma mouse trypanosomicide
INDEX TERM: Trypanosoma cruzi
(infection by, inhibitors of)
INDEX TERM: 54824-17-8 54824-20-3 **69408-81-7**
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(trypanosomicidal activity of, in mice)

L7 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:532639 CAPLUS
DOCUMENT NUMBER: 95:132639
ENTRY DATE: Entered STN: 12 May 1984
TITLE: Synthesis and cytostatic activity of benz[de] **isoquinoline**-1,3-diones. Structure-activity relationships
AUTHOR(S): Brana, Miguel Fernandez; Sanz, Antonio Martinez; Castellano, Jose Maria; Roldan, Cristobal Martinez; Roldan, Cristina
CORPORATE SOURCE: Fac. Cienc. Quim., Univ. Complutense, Madrid, Spain
SOURCE: European Journal of Medicinal Chemistry (1981), 16(3), 207-12
CODEN: EJMCA5; ISSN: 0009-4374
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
OTHER SOURCE(S): CASREACT 95:132639
GRAPHIC IMAGE:



I

ABSTRACT:
Fifty-one isoquinolinediones I (R = NO2, NH2, Cl, OH, NHCO2Et, MeO, NHAc, H, CMe3; R1 = NMe2, NEt2, pyrrolidino, piperidino, morpholino, 1-ethyl-3-piperidino, 4-methyl-1-piperazinyl, etc.) were prepared in 11-95% yield. Thus, reaction of 3-nitro-1,8-naphthalic anhydride and H2N(CH2)2NMe2 gave 64% I (R = NO2, R1 = NMe2, n = 2). The biol. activity was maximum (inhibiting the growth of HeLa cells) when n = 2. The presence of terminal N is essential for cytostatic activity. Substitution of polar atoms, e.g., S or O, decreased the cytotoxic activity.

SUPPL. TERM: benzisoquinolinedione prepn cytostatic; structure activity benzisoquinolinedione

INDEX TERM: Neoplasm inhibitors
(benzisoquinolinediones, structure in relation to)

INDEX TERM: Molecular structure-biological activity relationship
(cytostatic, of benzisoquinolinediones)

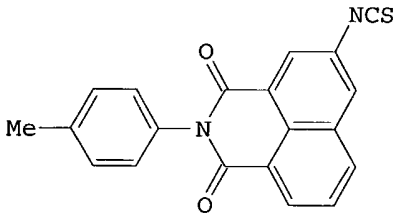
INDEX TERM: 54824-17-8P 54824-18-9P 54824-19-0P 54824-20-3P
69408-73-7P 69408-74-8P 69408-75-9P 69408-76-0P
69408-77-1P 69408-78-2P 69408-79-3P **69408-81-7P**
69408-82-8P 69408-83-9P
69408-84-0P 69408-85-1P
69408-86-2P 69408-87-3P
69408-88-4P 69408-89-5P 69408-90-8P
69408-91-9P 69408-92-0P 69408-93-1P 69408-94-2P
69408-95-3P 69408-96-4P 69408-97-5P 69408-98-6P
69408-99-7P 69409-00-3P 69409-01-4P 69409-02-5P
69409-03-6P 69409-05-8P 79070-55-6P 79070-56-7P
79070-57-8P 79070-58-9P 79070-59-0P 79070-60-3P
79070-61-4P 79070-62-5P 79070-63-6P 79070-64-7P
79070-65-8P 79070-66-9P 79070-67-0P 79070-68-1P
79070-69-2P 79070-70-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cytostatic activity of, structure in relation to)

INDEX TERM: 81-84-5 3027-38-1 5289-78-1 23204-36-6 23204-38-8
23921-27-9 69409-06-9 69409-08-1
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with amines, benzisoquinolinediones from)

INDEX TERM: 57-14-7 60-23-1 100-36-7 104-78-9 107-85-7
108-00-9 109-55-7 109-85-3 141-43-5, reactions
2038-03-1 4572-03-6 6789-94-2 7154-73-6 27578-60-5
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with naphthalic anhydrides, benzisoquinolinediones from)

L7 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:401943 CAPLUS
DOCUMENT NUMBER: 87:1943
ENTRY DATE: Entered STN: 12 May 1984
TITLE: 5-Isothiocyanato-1,8-naphthalenedicarboxy-4-methylphenylimide, a new fluorescence reagent for compounds containing amino groups
AUTHOR(S): Khalaf, Hosni; Rimpler, Manfred

CORPORATE SOURCE: Inst. Klin. Biochem. Physiol. Chem., Med. Hochsch. Hannover, Hannover, Fed. Rep. Ger.
SOURCE: Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie (1977), 358(4), 505-11
CODEN: HSZPAZ; ISSN: 0018-4888
DOCUMENT TYPE: Journal
LANGUAGE: German
CLASSIFICATION: 9-4 (Biochemical Methods)
OTHER SOURCE(S): CASREACT 87:1943
GRAPHIC IMAGE:



I

ABSTRACT:
5-Isothiocyanato-1,3-dioxo-2-p-tolyl-2,3-dihydro-1H-benz[de] ***isoquinoline*** (=5-isothiocyanato-1,8-naphthalenedicarbox-4-methylphenylimide) (I) was synthesized from 1H,3H-naphtho[1,8-cd]pyran-1,3-dione (=1.8-naphthalenedicarboxylic anhydride) through nitration, condensation with p-toluidine, reduction with SnCl2 yielding 5-amino-1,3-dioxo-2-p-tolyl-2,3-dihydro-1H-benz[de]**isoquinoline** as intermediate, and condensation with thiophosgene. I can be used for qual. and quant. analyses of compds. containing amino groups, including amino acids, amines, and proteins.

SUPPL. TERM: isothiocyanatodioxotolyldihydrobenzisoquinoline prepn; amino group fluorescence reagent prepn; amine fluorescence reagent prepn
INDEX TERM: Amino group
(determination of, with isothiocyanatonaphthalenedicarboxymethylphenylimide fluorescent reagent)
INDEX TERM: Amino acids, analysis
Proteins
ROLE: ANT (Analyte); ANST (Analytical study)
(determination of, with isothiocyanatonaphthalenedicarboxymethylphenylimide fluorescent reagent)
INDEX TERM: Fluorescence
(of isothiocyanatodioxotolyldihydrobenzisoquinoline, as amino group reagent)
INDEX TERM: Amines, analysis
ROLE: ANT (Analyte); ANST (Analytical study)
(biogenic, determination of, with isothiocyanatonaphthalenedicarboxymethylphenylimide fluorescent reagent)
INDEX TERM: **34418-98-9P** 62903-81-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and IR of)
INDEX TERM: 62903-82-6P
ROLE: PREP (Preparation)
(preparation of, as amino group fluorescent reagent)

L7 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1974:576158 CAPLUS
DOCUMENT NUMBER: 81:176158

ENTRY DATE: Entered STN: 12 May 1984
TITLE: Compositions for diabetic complications
INVENTOR(S): Sestanj, Kazimir; Simard-Duquesne, Nicole; Dvornik, Dusan M.
PATENT ASSIGNEE(S): Ayerst McKenna and Harrison Ltd.
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.: A61K
US PATENT CLASSIF.: 424258000
CLASSIFICATION: 63-6 (Pharmaceuticals)
Section cross-reference(s): 27
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3821383	A	19740628	US 1972-270357	19720710
PRIORITY APPLN. INFO.:			US 1972-270357	19720710

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 3821383	IC	A61K
	NCL	424258000

GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
Diabetes mellitus associated complications such as cataracts, neuropathy, nephropathy, and retinopathy in a diabetic mammal are prevented by administration of a composition containing I (X = 5-O2N, 5-H2N, or 6-Br). Thus, 1,8-naphthalic acid anhydride, glycine, and DMF are heated and stirred at reflux for 2 hr to give 1,3-dioxo-1H-benz[de]**isoquinoline**-2(3H)-acetic acid (I, X = H) 271-2°. Similarly prepared were (X and m.p. given): 6-Br, 279-81°; 5-O5N, 273-5°. Treatment of galactosemic or diabetic rats with the above compds. showed that the lenses of the treated rats contained significantly less (.apprx.35%) dulcitol than those of untreated rats. The compds. lessen the rate of formation of irreversible opacities and cataracts in the lenses of galactosemic rats and show a protective effect against the accumulation of dulcitol in the sciatic nerves of the galactosemic rats; this condition is analogous to the accumulation of sorbitol in advanced neuropathy. The compds. also decreased sorbitol accumulation in the lens and sciatic nerves and reduced the number of lenses with opacities normally expected to occur in diabetic rats.

SUPPL. TERM: diabetic complication benzisoquinolineacetate
INDEX TERM: Diabetes mellitus
(complications from, dioxobenzisoquinolineacetic acids for treatment of)
INDEX TERM: 51411-04-2 53497-33-9 53497-34-0 **53497-35-1**
ROLE: BIOL (Biological study)
(diabetic complications treatment with)
INDEX TERM: 81-84-5 81-86-7 3027-38-1
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with glycine)
INDEX TERM: 56-40-6, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(with naphthalic anhydrides)

L7 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1971:463498 CAPLUS
DOCUMENT NUMBER: 75:63498
ENTRY DATE: Entered STN: 12 May 1984
TITLE: Aminonaphthalimides
INVENTOR(S): Podrezova, T. N.; Reznichenko, V. V.; Plakidin, V. L.

SOURCE: U.S.S.R. From: Otkrytiya, Izobret., Prom. Obraztsy, Tovarnye Znaki 1970, 47(31), 26.
CODEN: URXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Russian
INT. PATENT CLASSIF.: C07D
CLASSIFICATION: 26 (Condensed Aromatic Compounds)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 283210		19701006	SU	19670918

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
SU 283210	IC	C07D

ABSTRACT:
Aminonaphthalimides were prepared by treating aminonaphthalic anhydride with an excess of liquid or solid primary amine in a 20-5% aqueous solution of NaHSO3 during
heating to 70-100°, with subsequent separation of the desired product.

SUPPL. TERM: naphthalimides amino
INDEX TERM: 1H-Benz[de]**isoquinoline**, derivs.
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
INDEX TERM: 1742-95-6P 10495-37-1P **23204-40-2P** 26558-87-2P
34418-97-8P **34418-98-9P 34419-01-7P**
34419-02-8P 34419-04-0P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

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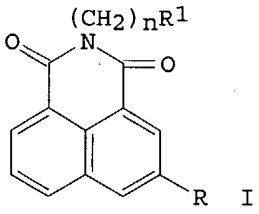
9/28/2004

ANSWER 1 OF 1 CASREACT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 95:132639 CASREACT
TITLE: Synthesis and cytostatic activity of benz[de]isoquinoline-1,3-diones. Structure-activity relationships
AUTHOR(S): Brana, Miguel Fernandez; Sanz, Antonio Martinez; Castellano, Jose Maria; Roldan, Cristobal Martinez; Roldan, Cristina
CORPORATE SOURCE: Fac. Cienc. Quim., Univ. Complutense, Madrid, Spain
SOURCE: European Journal of Medicinal Chemistry (1981), 16(3), 207-12
CODEN: EJMCA5; ISSN: 0009-4374
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
GRAPHIC IMAGE:



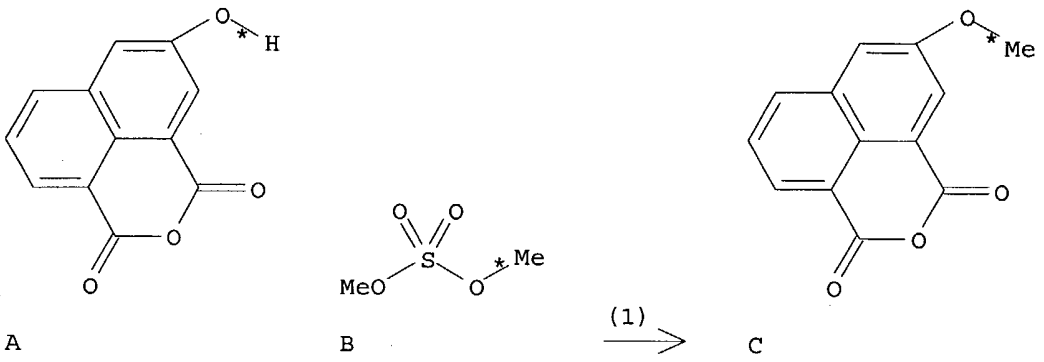
I

ABSTRACT:
Fifty-one isoquinolinediones I (R = NO2, NH2, Cl, OH, NHCO2Et, MeO, NHAc, H, CMe3; R1 = NMe2, NEt2, pyrrolidino, piperidino, morpholino, 1-ethyl-3-piperidino, 4-methyl-1-piperazinyl, etc.) were prepared in 11-95% yield. Thus, reaction of 3-nitro-1,8-naphthalic anhydride and H2N(CH2)2NMe2 gave 64% I (R = NO2, R1 = NMe2, n = 2). The biol. activity was maximum (inhibiting the growth of HeLa cells) when n = 2. The presence of terminal N is essential for cytostatic activity. Substitution of polar atoms, e.g., S or O, decreased the cytotoxic activity.

SUPPL. TERM: benzisoquinolinedione prepn cytostatic; structure activity benzisoquinolinedione
INDEX TERM: Neoplasm inhibitors
(benzisoquinolinediones, structure in relation to)
INDEX TERM: Molecular structure-biological activity relationship
(cytostatic, of benzisoquinolinediones)
INDEX TERM: 54824-17-8P 54824-18-9P 54824-19-0P 54824-20-3P
69408-73-7P 69408-74-8P 69408-75-9P 69408-76-0P
69408-77-1P 69408-78-2P 69408-79-3P 69408-81-7P
69408-82-8P 69408-83-9P 69408-84-0P 69408-85-1P
69408-86-2P 69408-87-3P 69408-88-4P 69408-89-5P
69408-90-8P 69408-91-9P 69408-92-0P 69408-93-1P
69408-94-2P 69408-95-3P 69408-96-4P 69408-97-5P
69408-98-6P 69408-99-7P 69409-00-3P 69409-01-4P
69409-02-5P 69409-03-6P 69409-05-8P 79070-55-6P
79070-56-7P 79070-57-8P 79070-58-9P 79070-59-0P
79070-60-3P 79070-61-4P 79070-62-5P 79070-63-6P
79070-64-7P 79070-65-8P 79070-66-9P 79070-67-0P
79070-68-1P 79070-69-2P 79070-70-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cytostatic activity of, structure in relation to)
INDEX TERM: 81-84-5 3027-38-1 5289-78-1 23204-36-6 23204-38-8
23921-27-9 69409-06-9 69409-08-1

INDEX TERM: ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with amines, benzisoquinolinediones from)
57-14-7 60-23-1 100-36-7 104-78-9 107-85-7
108-00-9 109-55-7 109-85-3 141-43-5, reactions
2038-03-1 4572-03-6 6789-94-2 7154-73-6 27578-60-5
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with naphthalic anhydrides,
benzisoquinolinediones from)

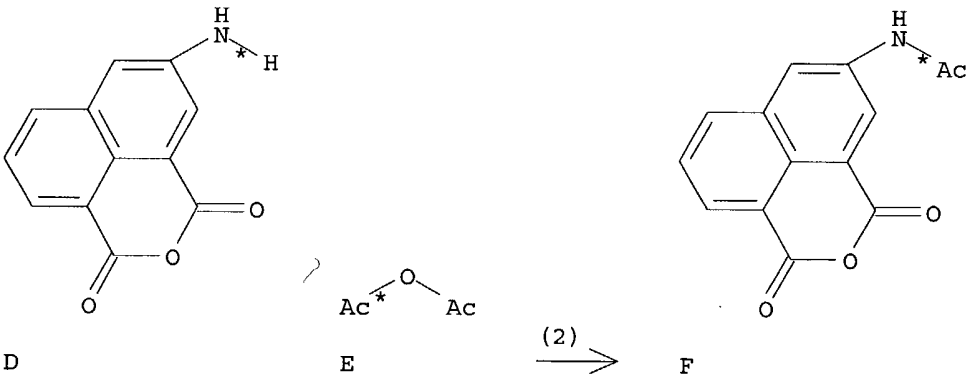
RX(1) OF 109 ...A + B ===> C...



A B (1) C

RX(1) RCT A 23204-36-6, B 77-78-1
PRO C 5289-78-1

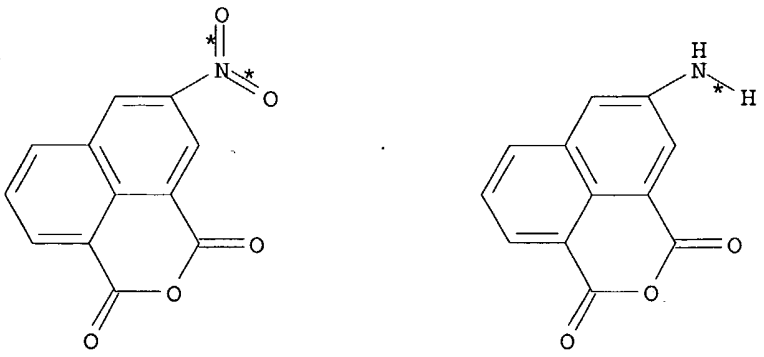
RX(2) OF 109 ...D + E ===> F...



D E (2) F

RX(2) RCT D 23204-38-8, E 108-24-7
PRO F 61690-44-6

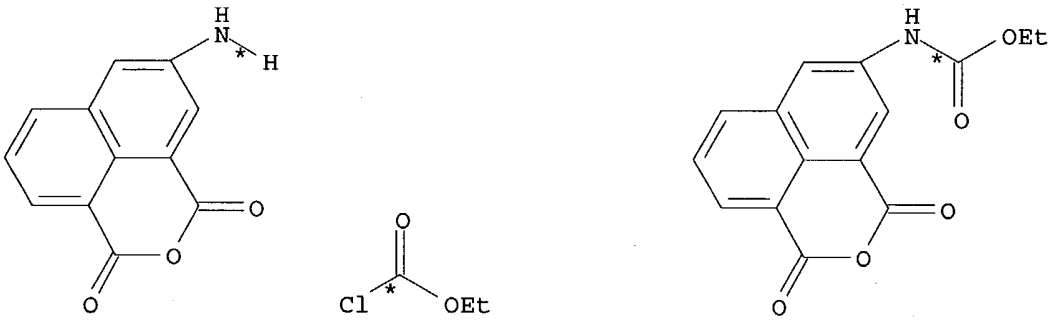
RX(3) OF 109 G ===> D...



G (3) D

RX(3) RCT G 3027-38-1
PRO D 23204-38-8

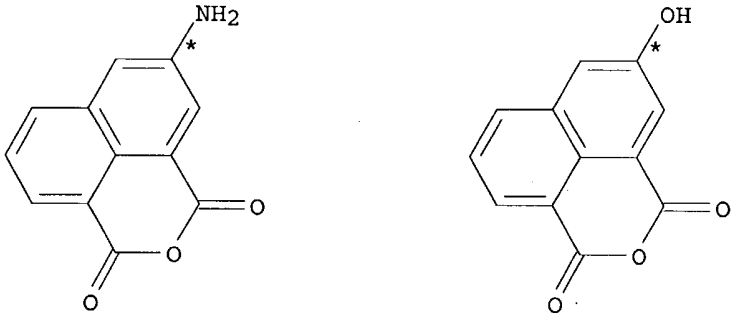
RX(4) OF 109 ...D + H ===> I...



D H (4) I

RX(4) RCT D 23204-38-8, H 541-41-3
PRO I 69409-06-9

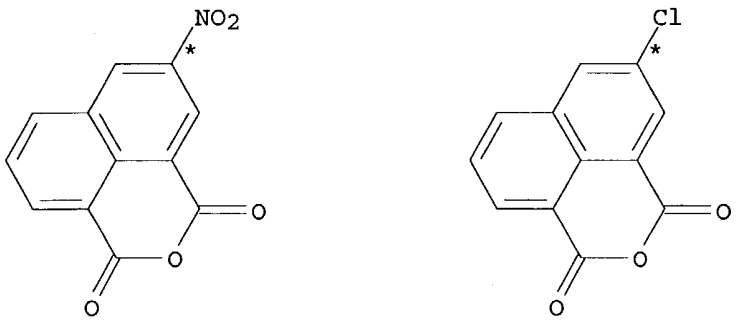
RX(5) OF 109 ...D ===> A...



D (5) A

RX(5) RCT D 23204-38-8
PRO A 23204-36-6

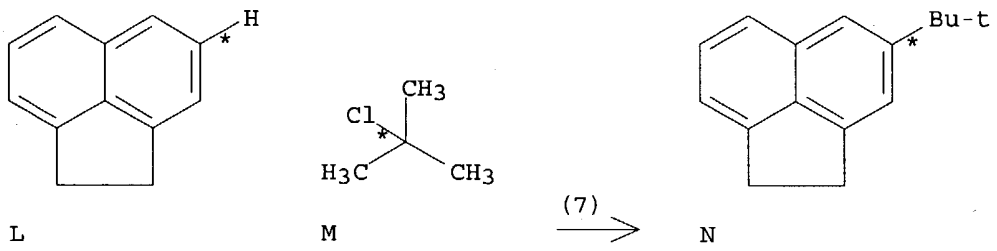
RX(6) OF 109 G ===> J...



G J

RX(6) RCT G 3027-38-1
RGT K 10026-13-8 PCl5
PRO J 23921-27-9

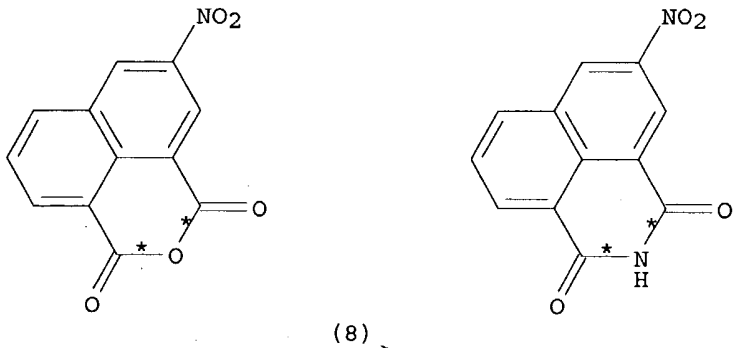
RX(7) OF 109 L + M ===> N



L M N

RX(7) RCT L 83-32-9, M 507-20-0
PRO N 55939-14-5

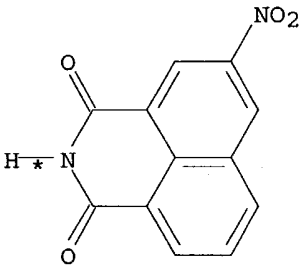
RX(8) OF 109 **G** ===> **O**...

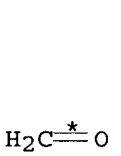


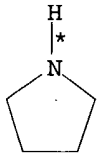
G O
YIELD 69%

RX(8) RCT G **3027-38-1**
RGT P 7664-41-7 NH3
PRO O **66266-36-2**

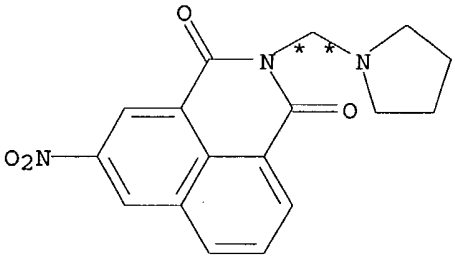
RX(9) OF 109 ...O + Q + R ===> S







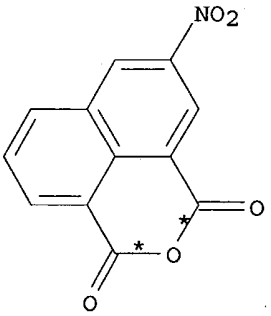
O Q R (9) →

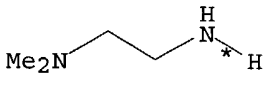


S
YIELD 20%

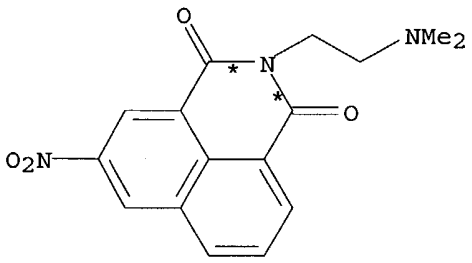
RX(9) RCT O 66266-36-2, Q 50-00-0, R 123-75-1
PRO S 79070-70-5

RX(10) OF 109 G + T ===> U





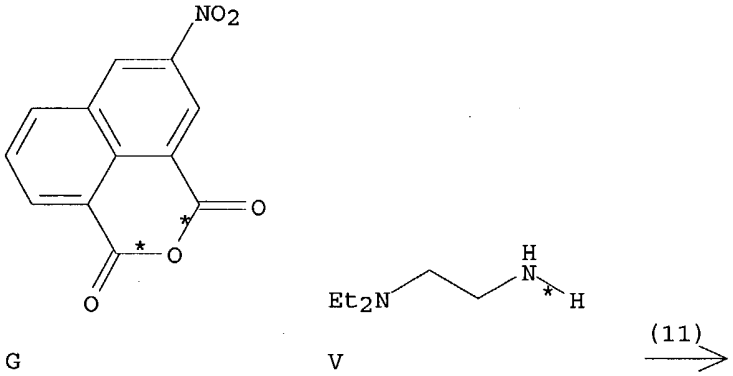
G T (10) →



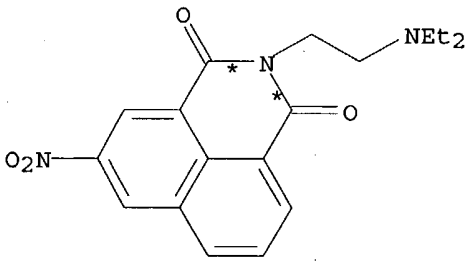
U
YIELD 64%

RX(10) RCT G 3027-38-1, T 108-00-9
PRO U 54824-17-8

RX(11) OF 109 G + V ===> W



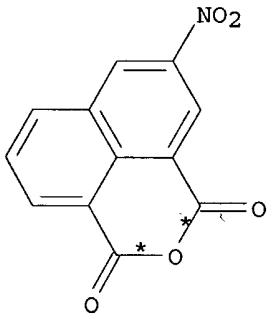
G V



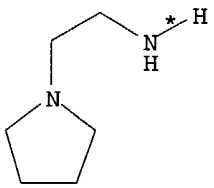
W
YIELD 64%

RX(11) RCT G 3027-38-1, V 100-36-7
PRO W 54824-18-9

RX(12) OF 109 G + X ===> Y

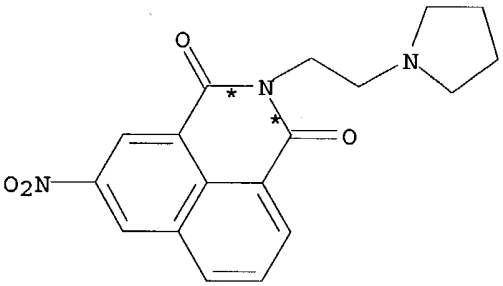


G



X

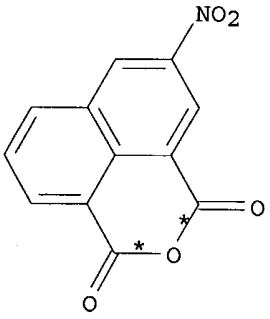
(12)



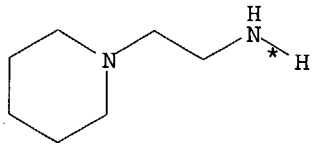
Y
YIELD 58%

RX(12) RCT G 3027-38-1, X 7154-73-6
PRO Y 54824-20-3

RX(13) OF 109 G + Z ===> AA

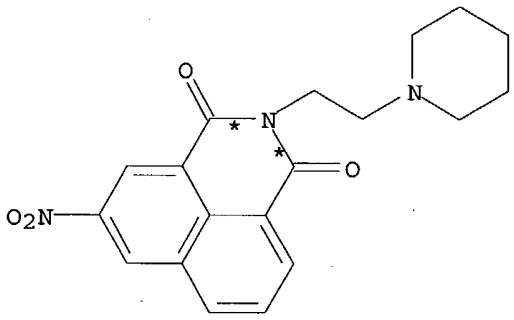


G



Z

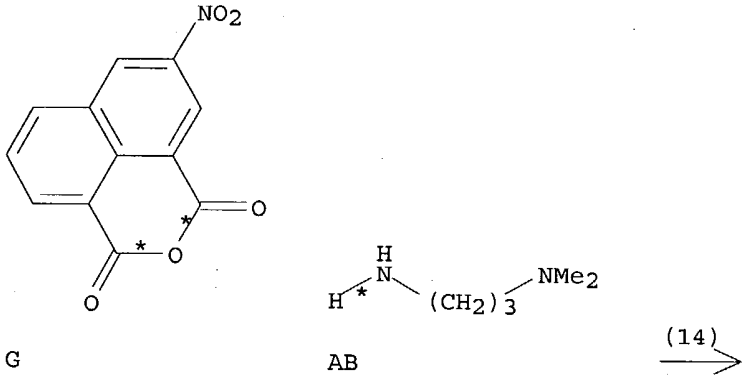
(13)



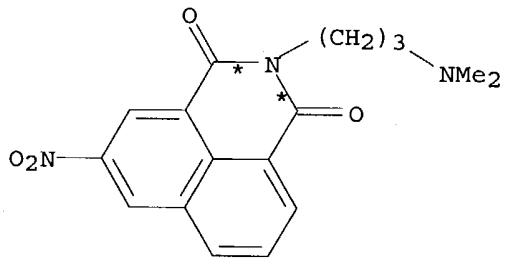
AA
YIELD 57%

RX(13) RCT G 3027-38-1, Z 27578-60-5
PRO AA 54824-19-0

RX(14) OF 109 G + AB ===> AC



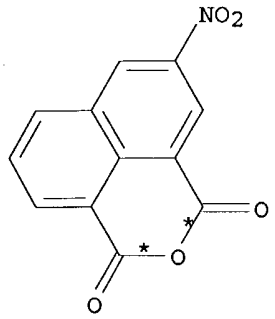
G AB

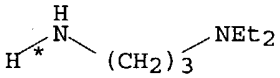


AC
YIELD 84%

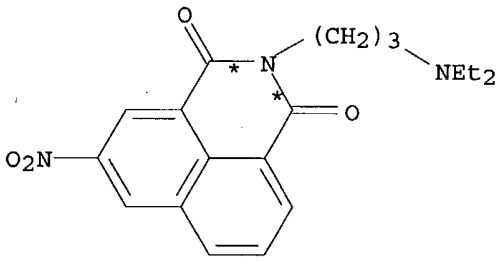
RX(14) RCT G 3027-38-1, AB 109-55-7
PRO AC 69408-73-7

RX(15) OF 109 G + AD ===> AE





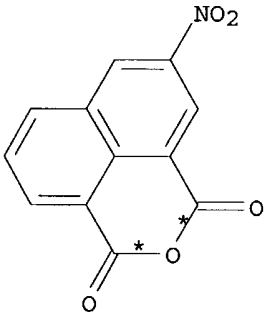
G AD (15) →

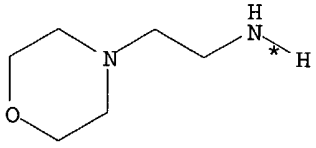


AE
YIELD 89%

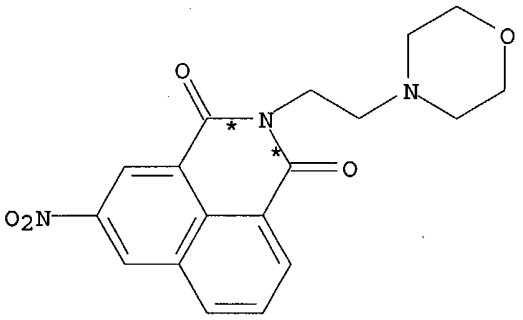
RX(15) RCT G 3027-38-1, AD 104-78-9
PRO AE 69408-74-8

RX(16) OF 109 G + AF ===> AG





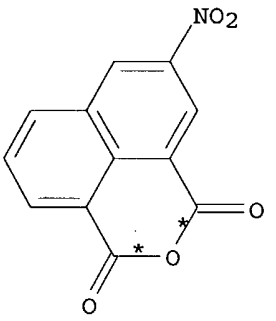
G AF (16) →



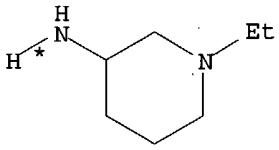
AG
YIELD 69%

RX(16) RCT G 3027-38-1, AF 2038-03-1
PRO AG 69408-75-9

RX(17) OF 109 G + AH ===> AI

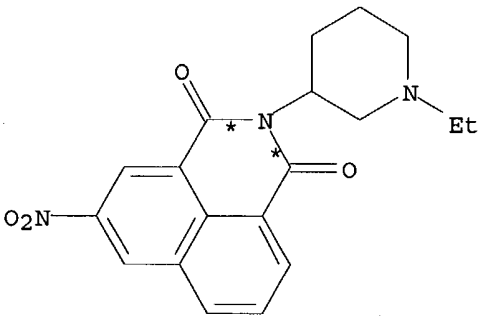


G



AH

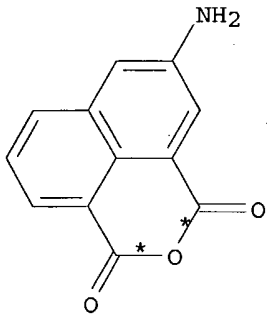
(17)

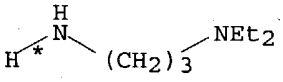


AI
YIELD 37%

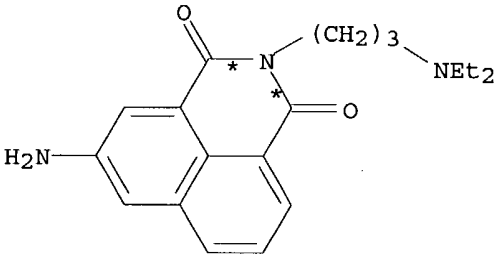
RX(17) RCT G 3027-38-1, AH 6789-94-2
PRO AI 69408-76-0

RX(18) OF 109 ...D + AD ===> AJ





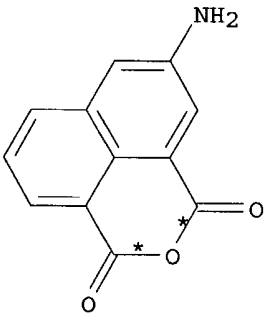
D AD (18)

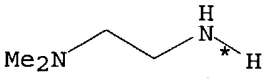


AJ
YIELD 81%

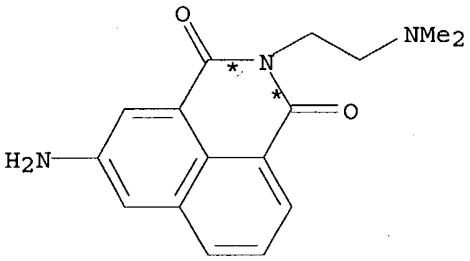
RX(18) RCT D 23204-38-8, AD 104-78-9
PRO AJ 69408-87-3

RX(19) OF 109 ...D + T ===> AK





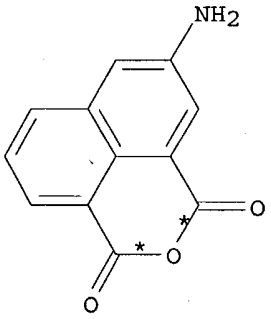
D T (19)



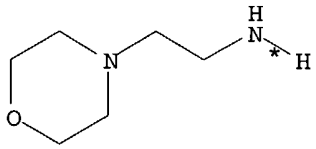
AK
YIELD 82%

RX(19) RCT D 23204-38-8, T 108-00-9
PRO AK 69408-81-7

RX(20) OF 109 ...D + AF ===> AL

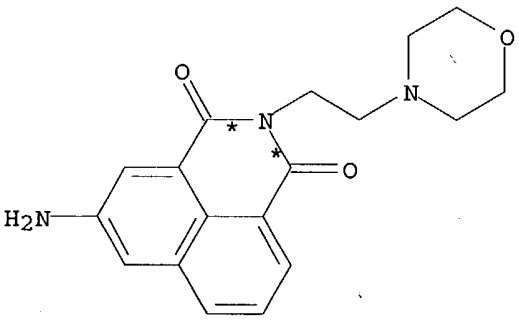


D



AF

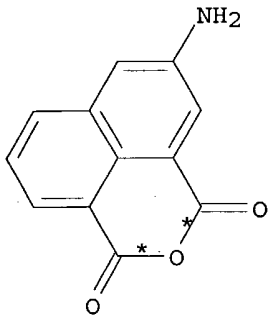
(20)



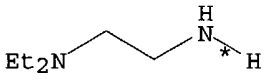
AL
YIELD 76%

RX(20) RCT D 23204-38-8, AF 2038-03-1
PRO AL 69408-85-1

RX(21) OF 109 ...D + V ===> AM

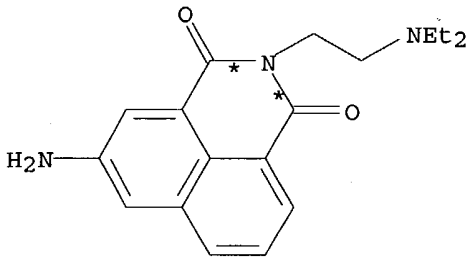


D



V

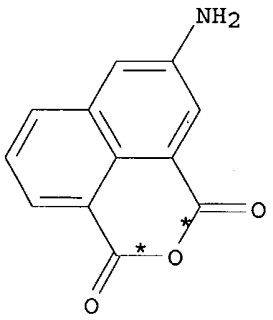
(21)



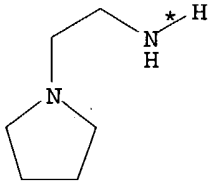
AM
YIELD 84%

RX(21) RCT D 23204-38-8, V 100-36-7
PRO AM 69408-82-8

RX(22) OF 109 ...D + X ===> AN

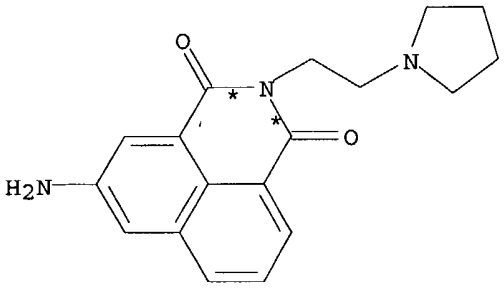


D



X

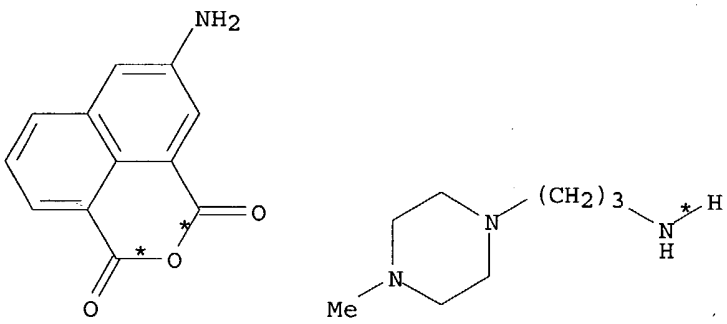
(22)



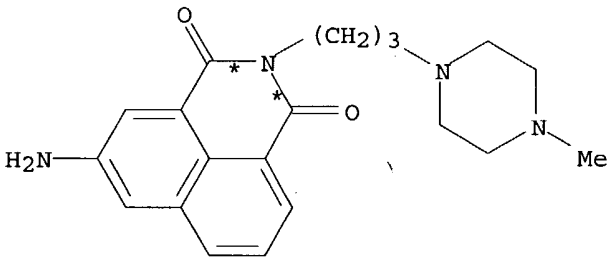
AN
YIELD 79%

RX(22) RCT D 23204-38-8, X 7154-73-6
PRO AN 69408-83-9

RX(23) OF 109 ...D + AO ===> AP



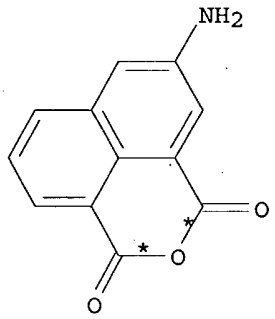
D AO (23)



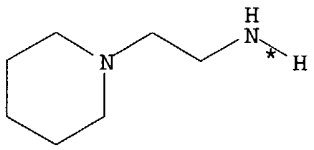
AP
YIELD 74%

RX(23) RCT D 23204-38-8, AO 4572-03-6
PRO AP 69408-88-4

RX(24) OF 109 ...D + Z ===> AQ

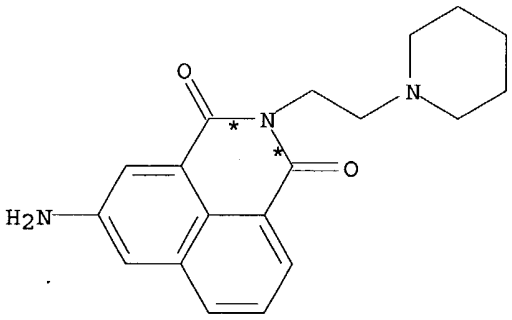


D



Z

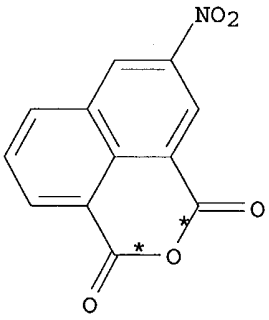
(24)



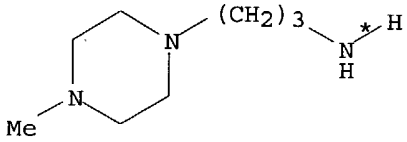
AQ
YIELD 75%

RX(24) RCT D 23204-38-8, Z 27578-60-5
PRO AQ 69408-84-0

RX(25) OF 109 G + AO ===> AR

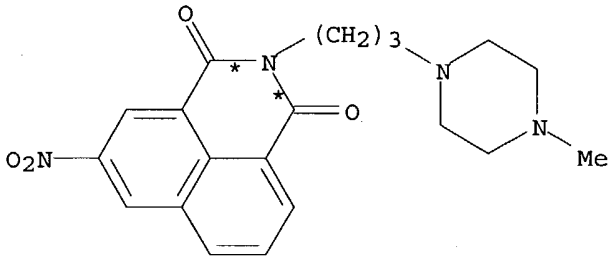


G



AO

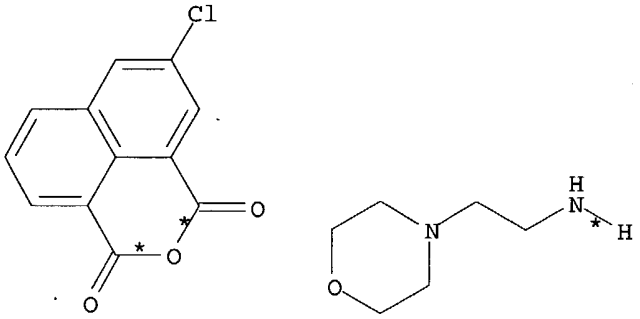
(25)



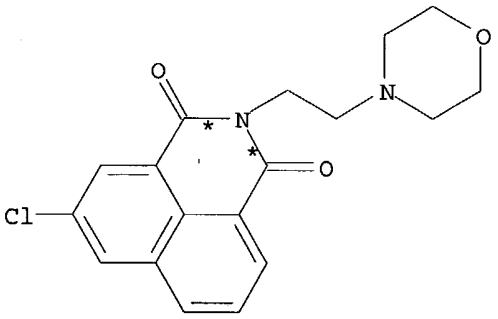
AR
YIELD 75%

RX(25) RCT G 3027-38-1, AO 4572-03-6
PRO AR 69408-77-1

RX(26) OF 109 ...J + AF ===> AS



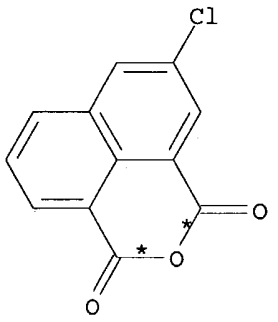
J AF (26)

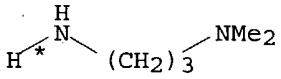


AS
YIELD 67%

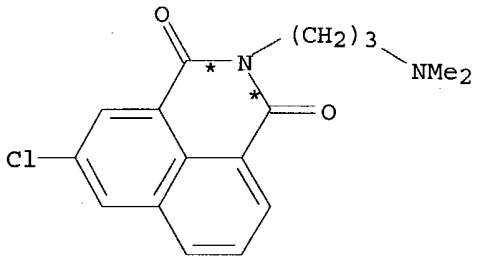
RX(26) RCT J 23921-27-9, AF 2038-03-1
PRO AS 69408-93-1

RX(27) OF 109 ...J + AB ===> AT





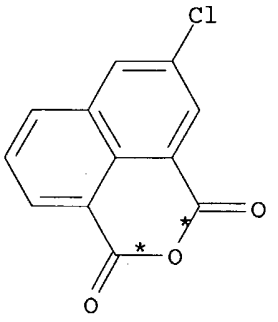
J AB (27) ⟶

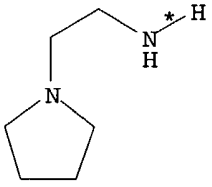


AT
YIELD 25%

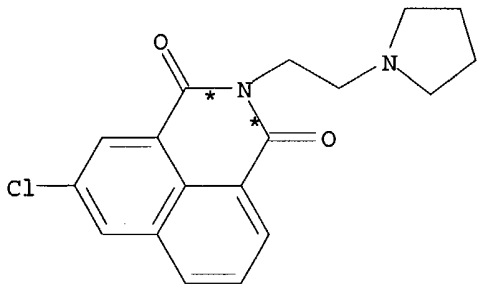
RX(27) RCT J 23921-27-9, AB 109-55-7
PRO AT 69408-94-2

RX(28) OF 109 ...J + X ===> AU





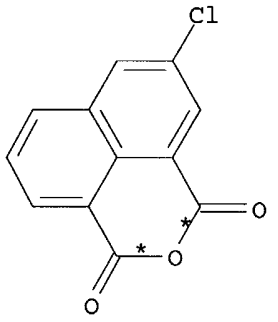
J X (28) ⟶



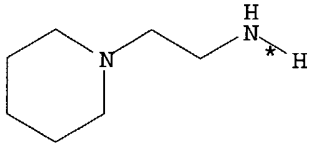
AU
YIELD 20%

RX(28) RCT J 23921-27-9, X 7154-73-6
PRO AU 69408-91-9

RX(29) OF 109 ...J + Z ===> AV

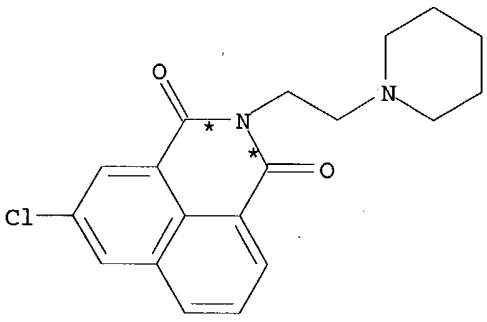


J



Z

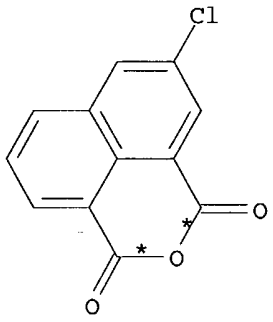
(29)

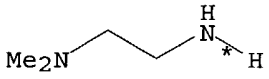


AV
YIELD 20%

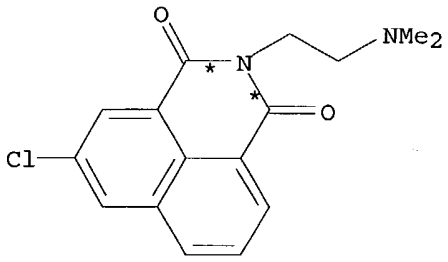
RX(29) RCT J 23921-27-9, Z 27578-60-5
PRO AV 69408-92-0

RX(30) OF 109 ...J + T ===> AW





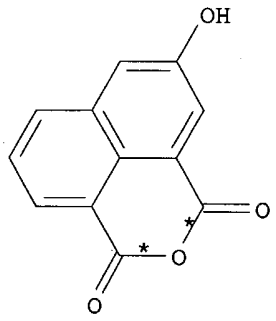
J T (30) ⟶

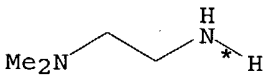


AW
YIELD 20%

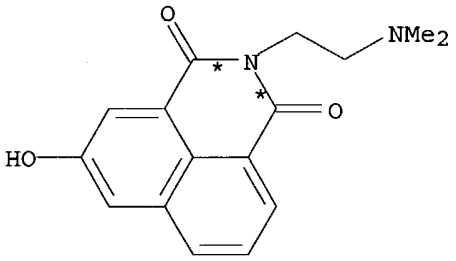
RX(30) RCT J 23921-27-9, T 108-00-9
PRO AW 69408-90-8

RX(31) OF 109 ...A + T ===> AX





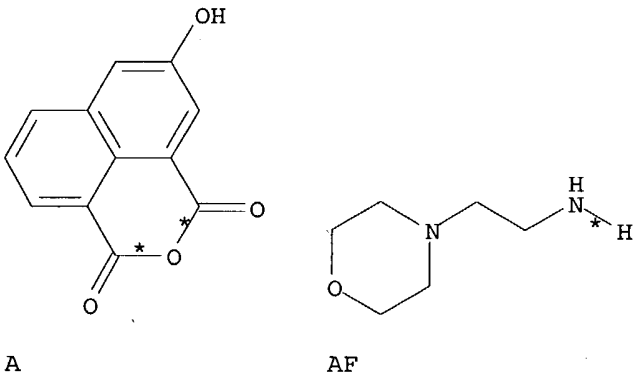
A T (31) ⟶



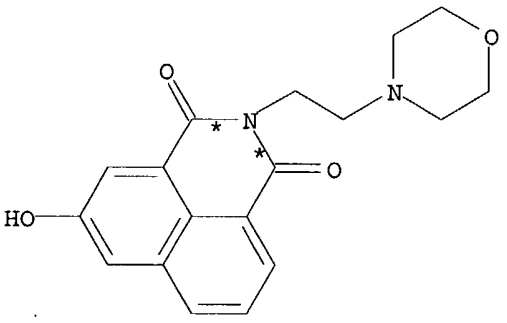
AX
YIELD 62%

RX(31) RCT A 23204-36-6, T 108-00-9
PRO AX 69408-95-3

RX(32) OF 109 ...A + AF ===> AY



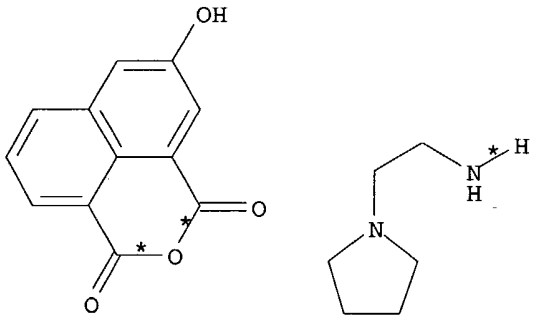
A AF (32)



AY
YIELD 27%

RX(32) RCT A 23204-36-6, AF 2038-03-1
PRO AY 69408-97-5

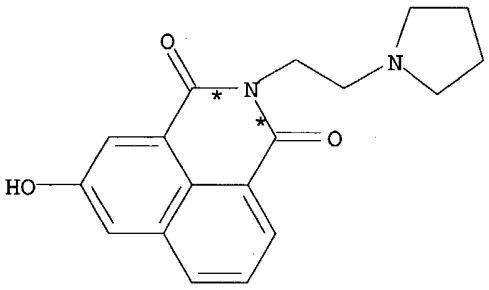
RX(33) OF 109 ...A + X ===> AZ



A

X

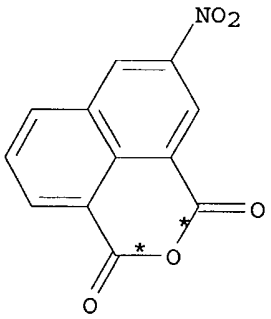
(33)



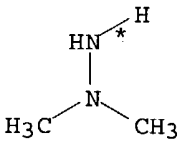
AZ
YIELD 81%

RX(33) RCT A 23204-36-6, X 7154-73-6
PRO AZ 69408-96-4

RX(34) OF 109 G + BA ===> BB

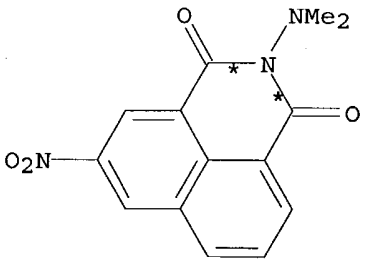


G



BA

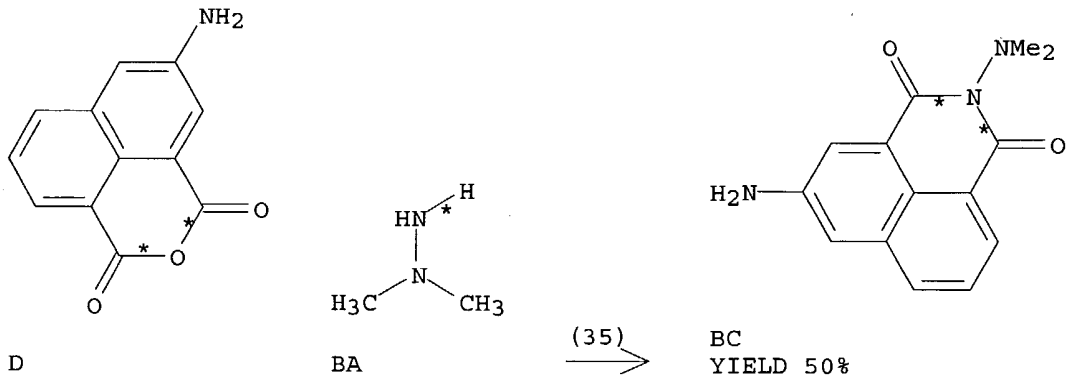
(34)



BB
YIELD 70%

RX(34) RCT G 3027-38-1, BA 57-14-7
PRO BB 69408-78-2

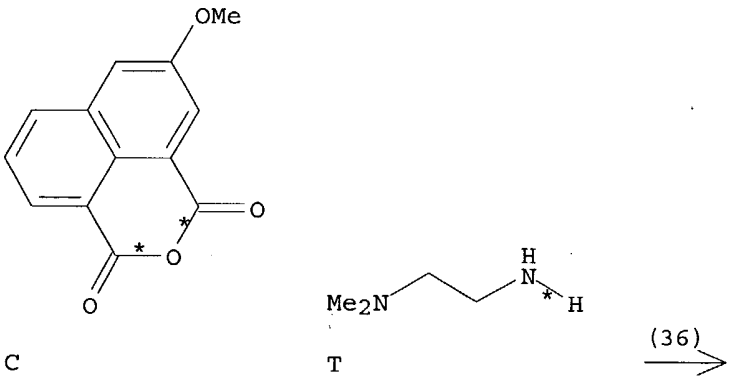
RX(35) OF 109 ...D + BA ===> BC



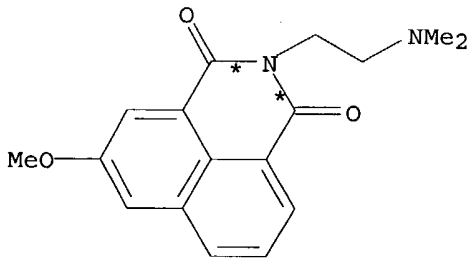
D BA BC
YIELD 50%

RX(35) RCT D 23204-38-8, BA 57-14-7
PRO BC 69408-89-5

RX(36) OF 109 ...C + T ===> BD



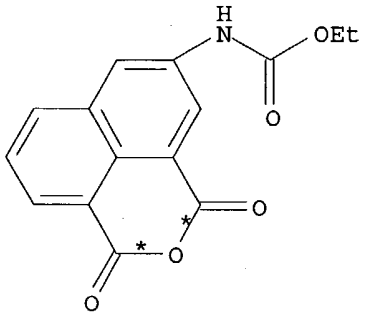
C T

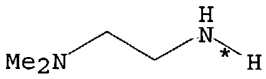


BD
YIELD 68%

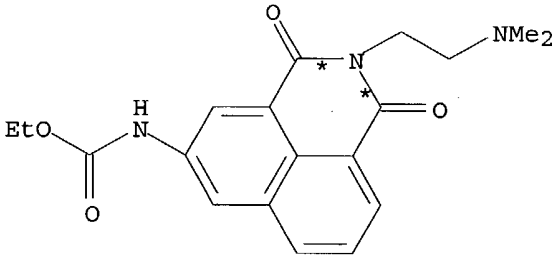
RX(36) RCT C 5289-78-1, T 108-00-9
PRO BD 69408-98-6

RX(37) OF 109 ...I + T ===> BE





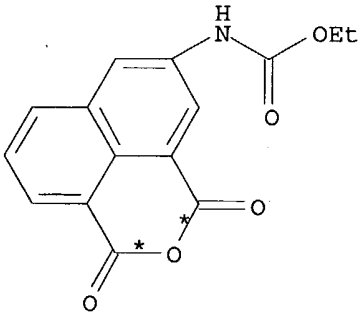
I T (37) →

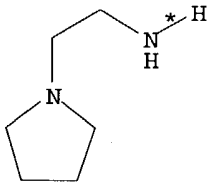


BE
YIELD 57%

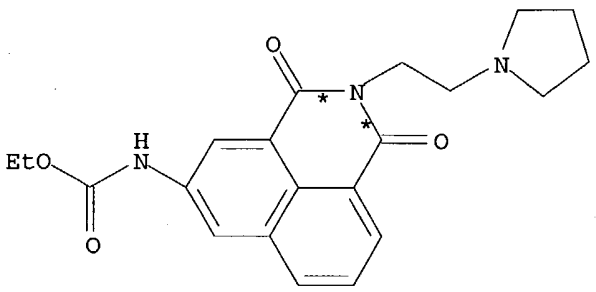
RX(37) RCT I 69409-06-9, T 108-00-9
PRO BE 69409-00-3

RX(38) OF 109 ...I + X ===> BF





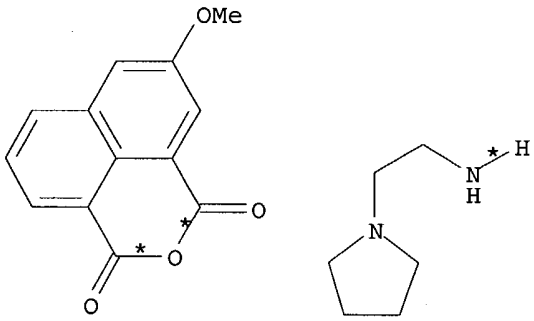
I X (38) →



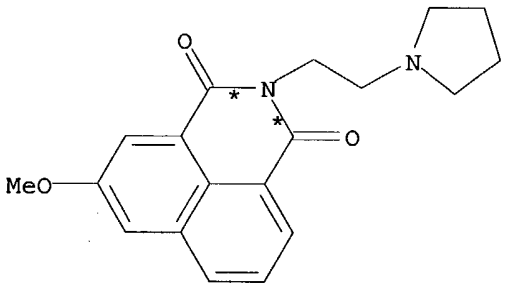
BF
YIELD 78%

RX(38) RCT I 69409-06-9, X 7154-73-6
PRO BF 69409-01-4

RX(39) OF 109 ...C + X ===> BG



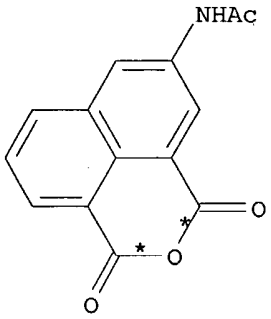
C X (39)

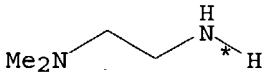


BG
YIELD 29%

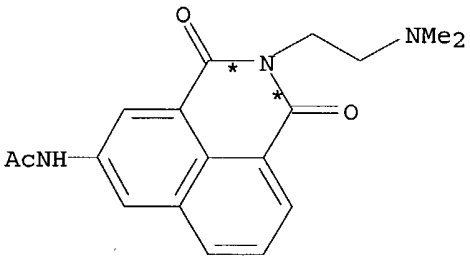
RX(39) RCT C 5289-78-1, X 7154-73-6
PRO BG 69408-99-7

RX(40) OF 109 ...F + T ===> BH





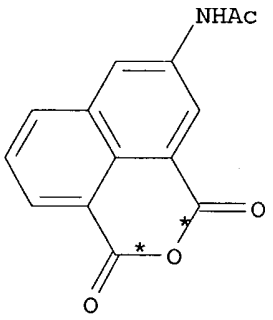
F T (40) ⟶

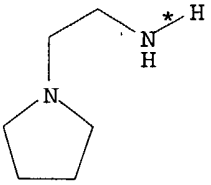


BH
YIELD 83%

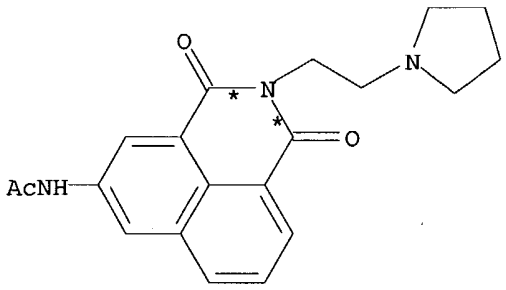
RX(40) RCT F 61690-44-6, T 108-00-9
PRO BH 69409-02-5

RX(41) OF 109 ...F + X ===> BI





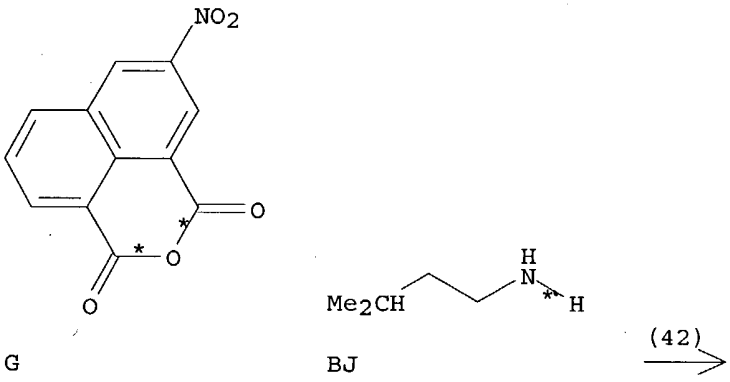
F X (41) ⟶



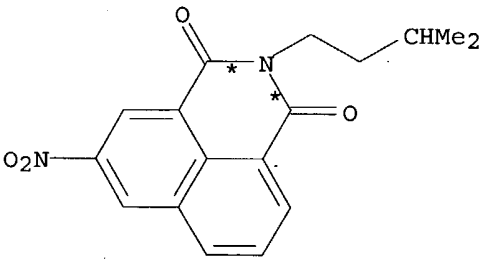
BI
YIELD 95%

RX(41) RCT F 61690-44-6, X 7154-73-6
PRO BI 69409-03-6

RX(42) OF 109 G + BJ ===> BK



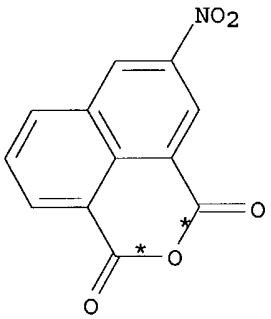
G BJ

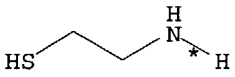


BK
YIELD 72%

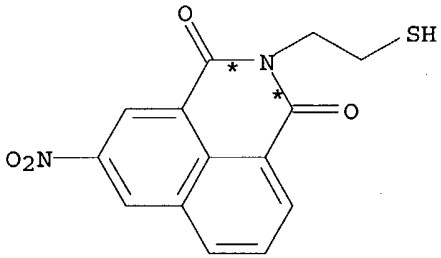
RX(42) RCT G 3027-38-1, BJ 107-85-7
PRO BK 79070-69-2

RX(43) OF 109 G + BL ===> BM





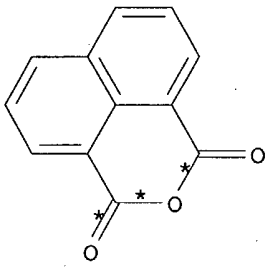
G BL (43)

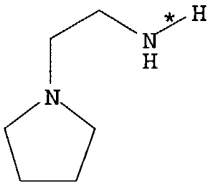


BM
YIELD 50%

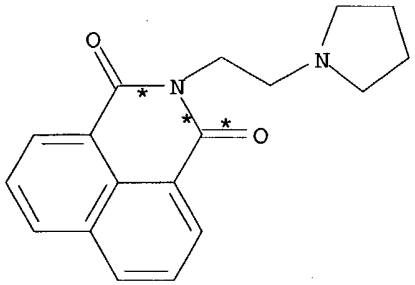
RX(43) RCT G 3027-38-1, BL 60-23-1
PRO BM 79070-68-1

RX(44) OF 109 BN + X ===> BO





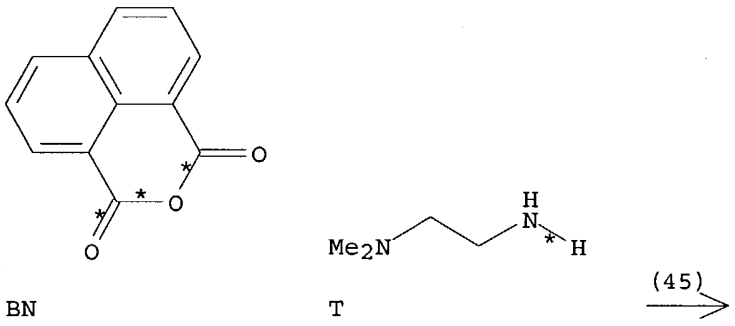
BN X (44)



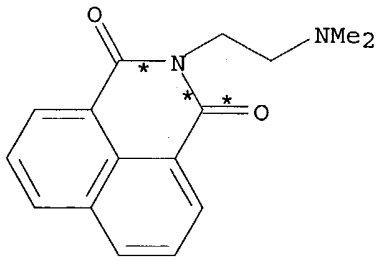
BO
YIELD 77%

RX(44) RCT BN 81-84-5, X 7154-73-6
PRO BO 79070-67-0

RX(45) OF 109 BN + T ===> BP



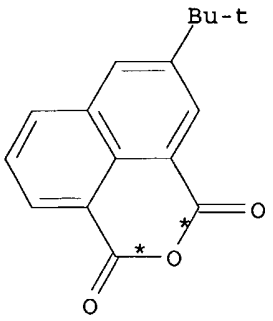
BN T

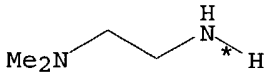


BP
YIELD 80%

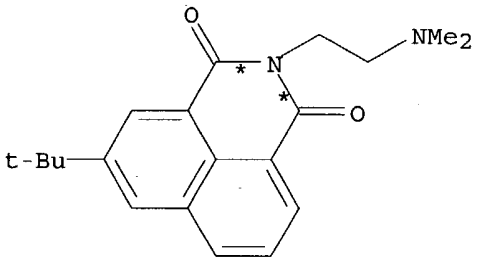
RX(45) RCT BN 81-84-5, T 108-00-9
PRO BP 79070-66-9

RX(46) OF 109 BQ + T ===> BR





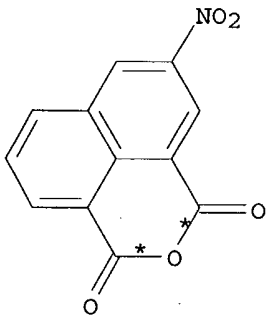
BQ T (46) ⟶

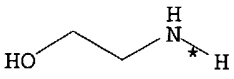


BR
YIELD 84%

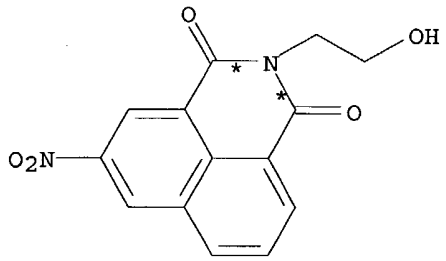
RX(46) RCT BQ 69409-08-1, T 108-00-9
PRO BR 69409-05-8

RX(47) OF 109 G + BS ===> BT





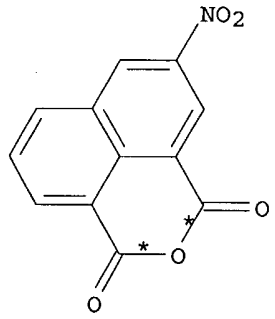
G BS (47) ⟶



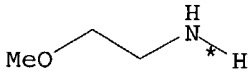
BT
YIELD 80%

RX(47) RCT G 3027-38-1, BS 141-43-5
PRO BT 79070-65-8

RX(48) OF 109 G + BU ===> BV

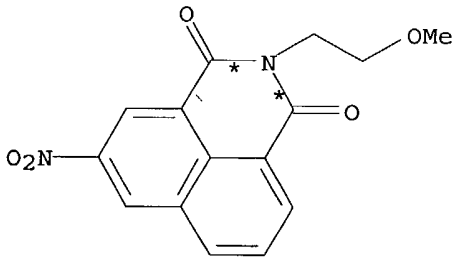


G



BU

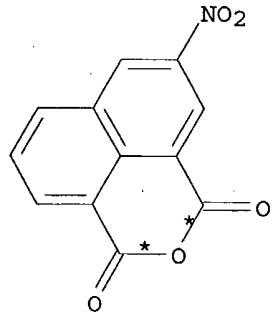
(48)



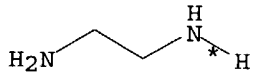
BV
YIELD 60%

RX(48) RCT G 3027-38-1, BU 109-85-3
PRO BV 79070-64-7

RX(49) OF 109 G + BW ===> BX...

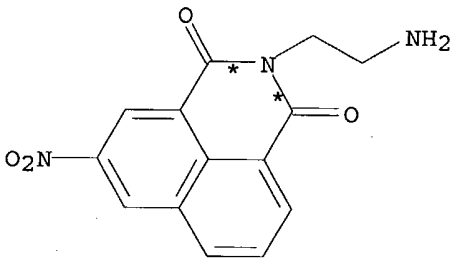


G



BW

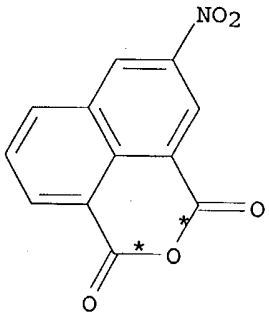
(49) →



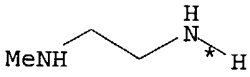
BX
YIELD 11%

RX(49) RCT G 3027-38-1, BW 107-15-3
PRO BX 79070-63-6

RX(50) OF 109 G + BY ===> BZ

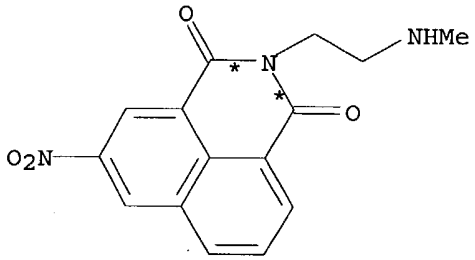


G



BY

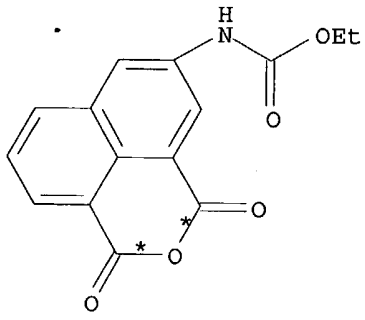
(50) →



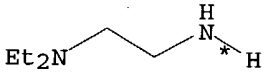
BZ
YIELD 49%

RX(50) RCT G 3027-38-1, BY 109-81-9
PRO BZ 79070-62-5

RX(51) OF 109 ...I + V ===> CA

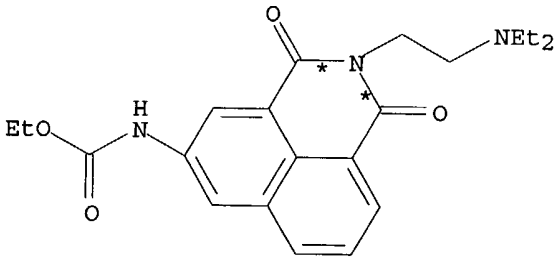


I



V

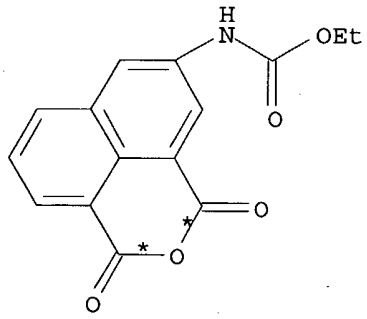
(51) →

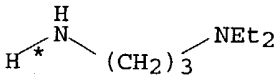


CA
YIELD 55%

RX(51) RCT I 69409-06-9, V 100-36-7
PRO CA 79070-60-3

RX(52) OF 109 ...I + AD ===> CB

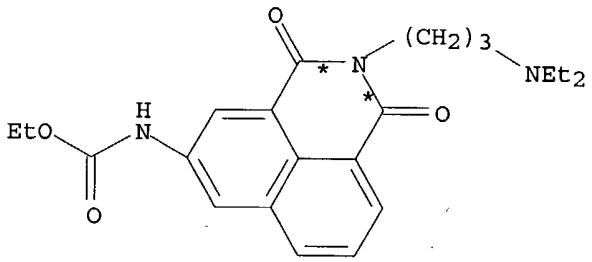




I

AD

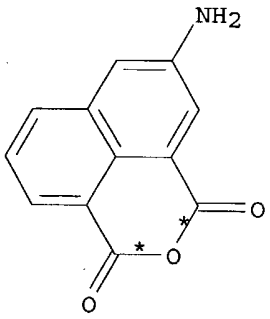
(52)

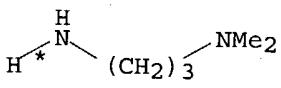


CB
YIELD 57%

RX(52) RCT I 69409-06-9, AD 104-78-9
PRO CB 79070-59-0

RX(53) OF 109 ...D + AB ===> CC

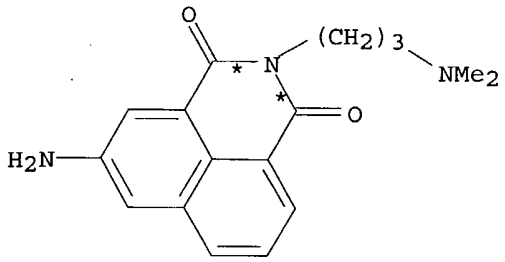




D

AB

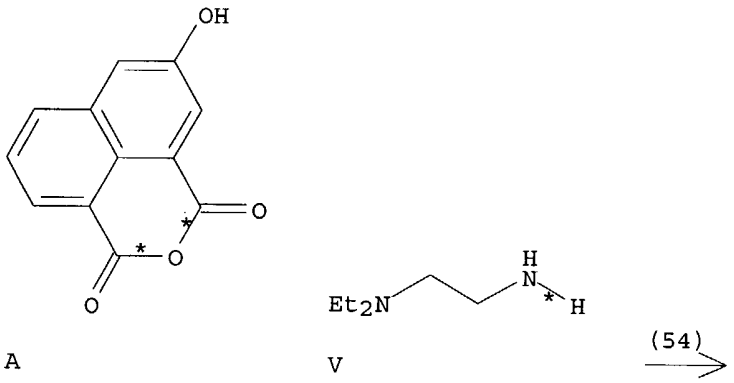
(53)



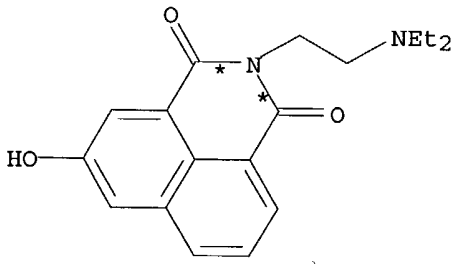
CC
YIELD 90%

RX(53) RCT D 23204-38-8, AB 109-55-7
PRO CC 69408-86-2

RX(54) OF 109 ...A + V ===> CD



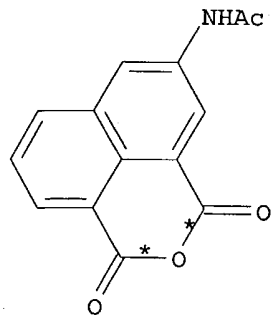
A V



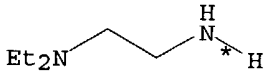
CD
YIELD 60%

RX(54) RCT A 23204-36-6, V 100-36-7
PRO CD 79070-58-9

RX(55) OF 109 ...F + V ===> CE

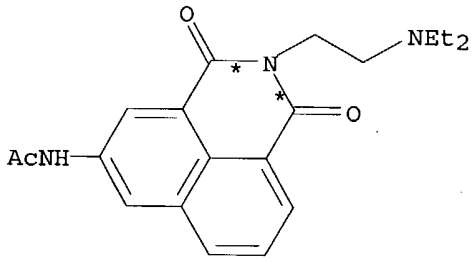


F



V

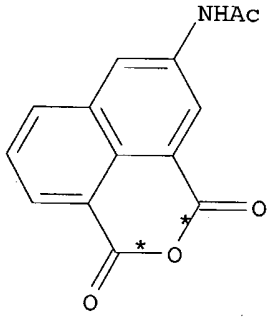
(55) →



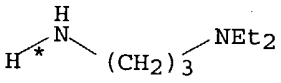
CE
YIELD 85%

RX(55) RCT F 61690-44-6, V 100-36-7
PRO CE 79070-57-8

RX(56) OF 109 ...F + AD ===> CF

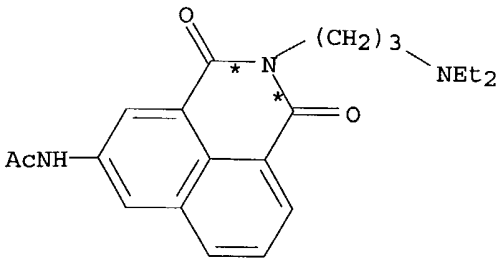


F



AD

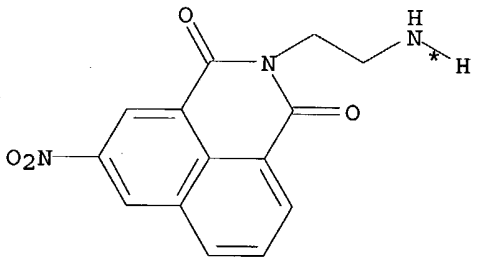
(56) →



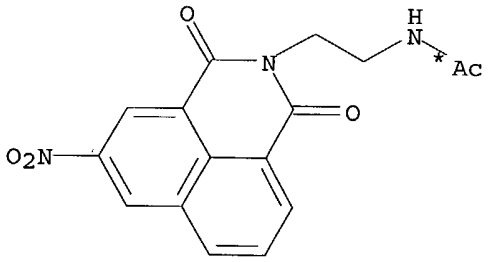
CF
YIELD 80%

RX(56) RCT F 61690-44-6, AD 104-78-9
PRO CF 79070-56-7

RX(57) OF 109 ...BX ===> CG



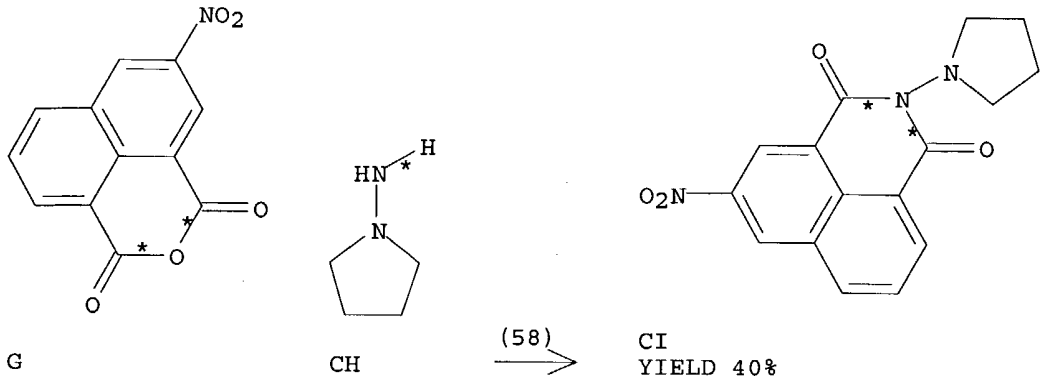
BX (57) ⟶



CG
YIELD 91%

RX(57) RCT BX 79070-63-6
PRO CG 79070-61-4

RX(58) OF 109 G + CH ===> CI



G CH CI
YIELD 40%

RX(58) RCT G 3027-38-1, CH 16596-41-1
PRO CI 69408-79-3

=>